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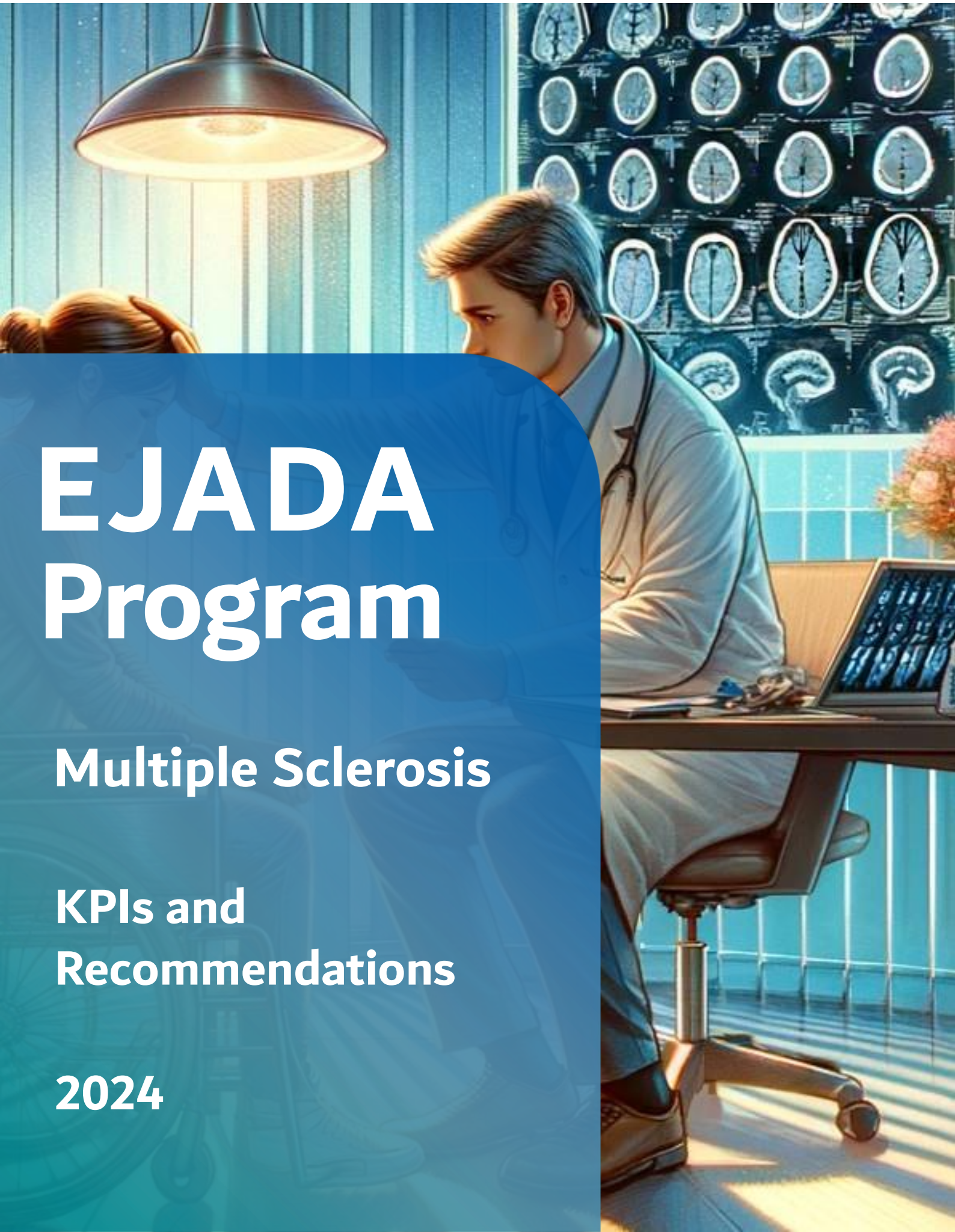
DUBAI HEALTH AUTHORITY

إجادة
EJADA



EJADA Program

Multiple Sclerosis

KPIs and Recommendations

2024

Multiple Sclerosis

KPIs and Recommendations

Content

Introduction

Multiple Sclerosis (MS) is a chronic demyelinating disorder of the central nervous system (CNS) that affects predominately patients aged 20-40 years. The epidemiology of MS is changing worldwide, as the understanding of its immunopathogenesis and natural history, with new evidence pointing towards a multifactorial etiology involving both environmental and genetic factors. The prevalence and incidence rates of MS have been steadily increasing worldwide over the last few decades including the Middle East North Africa (MENA) region. The field of MS therapeutics is evolving rapidly as several novel disease modifying therapies (DMTs) have been added to our armamentarium in the last decade. There is a clear need to unify and update the diagnostic and therapeutic paradigms in Dubai as: Most countries in the region are in the process of establishing specialized MS centers.

1. Some diagnostic mimickers of MS, such as neurobrucellosis, neuro-Behçet, Toxocara canis myelitis, Human T-lymphotropic virus 1 (HTLV-1) myelitis, and others might be unique or much more common in the Middle East compared to Europe or North America, which necessitates a slightly different diagnostic approach.
2. With evolving diagnostic criteria and the advent of new oral and parenteral therapies for multiple sclerosis (MS), most current diagnostic and treatment algorithms need revision and updating.
3. The diagnosis of MS relies on incorporating clinical and paraclinical findings to prove dissemination in space and time and exclude alternative diseases that can explain the findings at hand. The differential diagnostic workup should be guided by clinical and laboratory red flags to avoid unnecessary tests.
4. Appropriate selection of MS therapies is critical to maximize patient benefit.

The current guidelines review the current diagnostic criteria for MS and the scientific evidence supporting treatment of acute relapses, radiologically isolated syndrome, clinically isolated syndrome, relapsing remitting MS, progressive MS, pediatric cases and pregnant women. The purpose of these guidelines is to provide practical recommendations and algorithms for the diagnosis and treatment of MS based on current scientific evidence and clinical experience.

Scope

The Ejada KPIs are quality indicators and ratings for physicians, facilities and insurance com- panies based on information collected by DHA systems from providers, payers and patients. This document has been formulated in accordance with the Consensus recommendations for the diagnosis and treatment of multiple sclerosis: 2023 revisions of the MENACTRIMS guidelines and the NMSS Disease Modifying Treatment Guidelines for Multiple Sclerosis in the United Arab Emirates. Any future revisions to the aforementioned guidelines will prompt a corresponding update to this document.

To ensure accuracy and coherence, this document consolidates various sources, addressing contradictions, incorporating updates, and incorporating additional information where nec- essary. These sources include:

1. Multiple sclerosis in adults: management - NICE guideline - Published: 22 June 2022. www.nice.org.uk/guidance/ng220
2. Practice guideline recommendations summary: Disease-modifying therapies for adults with multiple sclerosis. Report of the Guideline Development, Dissemination, and Im- plementation Subcommittee of the American Academy of Neurology – Published: 2018 - Neurology® 2018;90:777-788. doi:10.1212/WNL.0000000000005347
3. ECTRIMS/EAN Guideline on the pharmacological treatment of people with multiple sclerosis. Multiple Sclerosis Journal 2018, Vol. 24(2) 96–120. DOI: 10.1177/1352458517751049. ©2018 European Academy of Neurology and Euro- pean Committee of Treatment of Research in Multiple Sclerosis.
4. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol 2018; 17: 162–73. Published Online December 21, 2017. http://dx.doi.org/10.1016/ S1474-4422(17)30470-2
5. 2021 MAGNIMS–CMSC–NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis. Lancet Neurol 2021; 20: 653–70. Published Online June 14, 2021. https://doi.org/10.1016/S1474-4422(21)00095-8

List of Abbreviations

S.No.	Abbreviation	Full form
1	AHSCT	Autologous haemopoeitic stem cells transplantation
2	ALZ	Alemtuzumab
3	CIS	Clinically isolated syndrome
4	CLAD	Cladribine
5	CNS	Central nervous system
6	CSF	Cerebrospinal fluid
7	DHA	Dubai Health Authority
8	DMF	Dimethyl fumarate
9	DIS	Dissemination in space
10	DIT	Dissemitation in time
11	DMT	Disease modifying therapy
12	dT	Diphtheria-Tetanus vaccine
13	dTap	Diphtheria-Tetanus-Pertusssis vaccine
14	EAN	European Association of Neurologists
15	ECTRIMS	European Committee for Treatment & Research in MS
16	GA	Glatiramer acetate
17	IFN	Interferon
18	IS	Immunosuppression
19	JVC	John Cunninghm Virus
20	MAGNIMS	Magnetic Resonance Imaging in MS
21	MENACTRIMS	MENA Committee for Treatment & Research in MS
22	MMR	Mumps-Measles-Rubella
23	MS	Multiple sclerosis
24	NEDA	No evidence of disease activity
25	NICE	National Institure for Clinical Excellence
26	NMSS	National multiple sclerosis society
27	NTZ	Natalizumab
28	PCV	Pneumococcal conjugate vaccine
29	PML	Progressive multifocal leukoencephalopathy
30	PPMS	Primary progressive multiple sclerosis
31	PPV	Pneumococcal polysaccharide vaccine
32	READ	Rapidly evolving aggressive disease
33	RIS	Radiologically isolated syndrome
34	RRMS	Relapsing-remitting multiple sclerosis
35	S1P	Sphingosine-1-phosphate

KPIs and their Measuring Parameters

Data collection frequency: Monthly

S.No.	KPIs	Measuring Parameters
1	Percentage of patients meeting the NEDA- 3 criteria	MRI, EDSS
2	Percentage of patients meeting the NEDA- 4 criteria	MRI, EDSS
3	Baseline EDSS	EDSS
4	Time to diagnosis	Medical records
5	MRI Progression	MRI
6	MRI monitoring for patients with MS	MRI
7	Bladder, Bowel, and Sexual Dysfunction Screening and Follow-Up for Patients with MS	Urology referral, Internal medicine referral, GIT referral
8	Cognitive Impairment Screening and Fol- low-Up for Patients with Multiple Sclerosis (MS)	Neuropsycholist referral, Psy- chologist referral, Speech/lan- guage pathologist referral, Occupational therapist referral
9	Fatigue Screening and Follow-Up for Pa- tients with MS	The Fatigue Severity Scale (FSS), Modified Fatigue Impact Scale, Shortened Modified Fatigue Impact Scale, Treatment plan, referral to PT/OT, exercise pro- gram, lifestyle modification pro- gram, or referral to an appropri- ate healthcare provider.

Diagnosis of multiple sclerosis

People with multiple sclerosis may present with a positive history of a relapse/attack. A re-lapse or attack is defined as follows:

- **Attack**: Attack, relapse, exacerbation, and (when it is the first episode) clinically isolat- ed syndrome are synonyms. See clinically isolated syndrome and relapse for descrip- tions.
- **Clinically Isolated Syndrome**: A monophasic clinical episode with patient-reported symptoms and objective findings reflecting a focal or multifocal inflammatory demye- linating event in the CNS, developing acutely or subacutely, with a duration of at least 24 h, with or without recovery, and in the absence of fever or infection (similar to a typical multiple sclerosis relapse (attack and exacerbation) but in a patient not known to have multiple sclerosis). A clinically isolated syndrome can be monofocal (reflecting pathology in a single location) or multifocal; the specific manifestations of a clinically isolated syndrome depend on the anatomical location (or locations) of the pathology. Typical presentations include unilateral optic neuritis, focal supratentorial syndrome, focal brainstem or cerebellar syndrome, or partial myelopathy; examples of atypical presentations include bilateral optic neuritis, complete ophthalmoplegia, complete myelopathy, encephalopathy, headache, alteration of consciousness, meningismus, or isolated fatigue.
- **Relapse**: A monophasic clinical episode with patient-reported symptoms and objec- tive findings typical of multiple sclerosis, reflecting a focal or multifocal inflammatory demyelinating event in the CNS, developing acutely or subacutely, with a duration of at least 24 h, with or without recovery, and in the absence of fever or infection. Attack, relapse, exacerbation, and (when it is the first episode) clinically isolated syndrome are synonyms.

People with multiple sclerosis (MS) may present with a wide range of symptoms affecting different parts of the body. The most common are:

1. Loss or reduction of vision in 1 eye with painful eye movements
2. Double vision
3. Ascending sensory disturbance and/or weakness
4. Altered sensation or pain travelling down the back and sometimes into the limbs when bending the neck forwards (Lhermitte's sign)
5. Progressive difficulties with balance and gait.

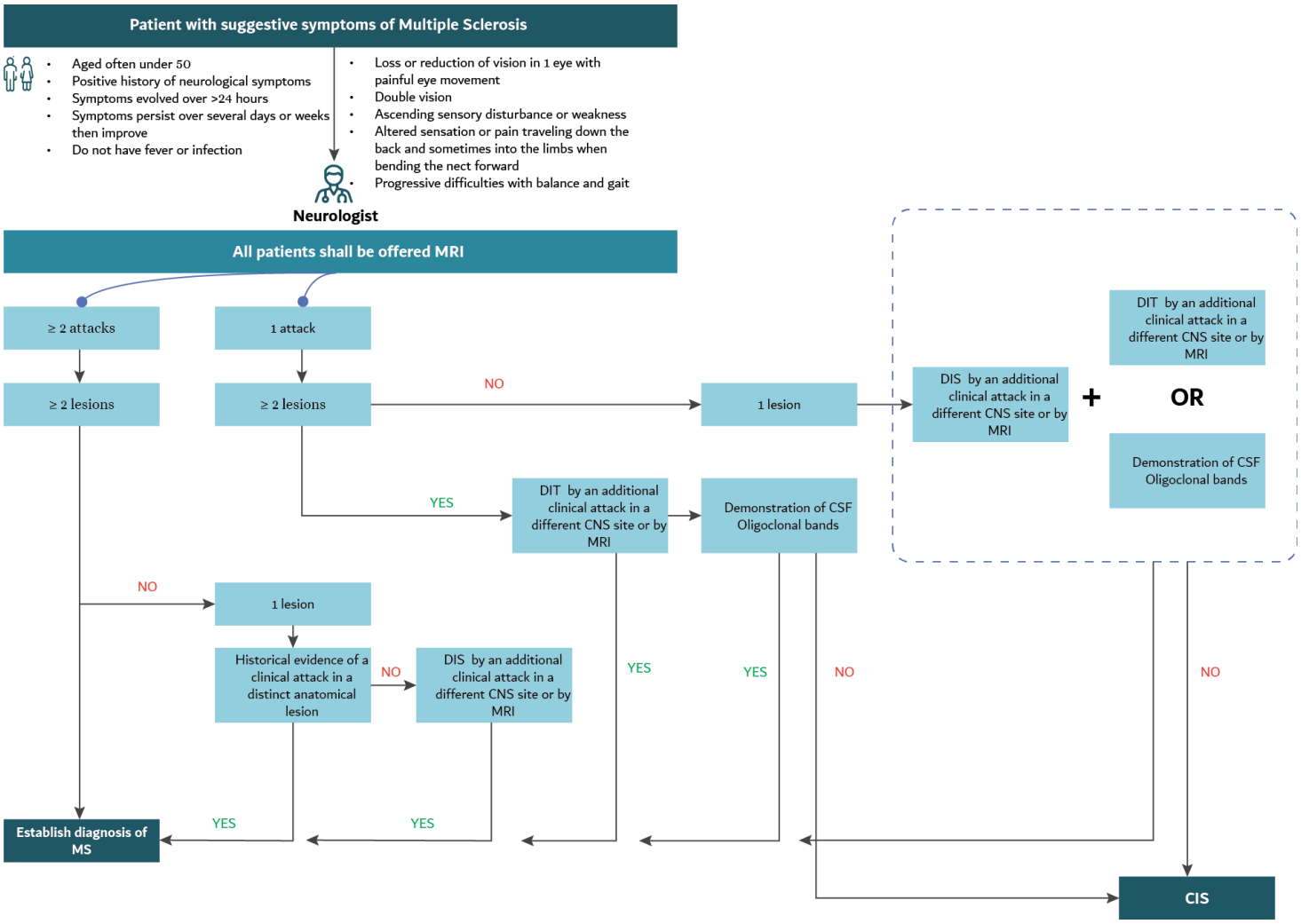
Usually, people with MS present with neurological symptoms or signs as described above are:

1. Are often aged under 50 and
2. May have a history of previous neurological symptoms and
3. Have symptoms that have evolved over more than 24 hours and
4. Have symptoms that may persist over several days or weeks and then improve and
5. Do not have fever or infection.
6. Do not routinely suspect MS if a person's main symptoms are fatigue, depression, dizziness, or vague sensory phenomena, unless they have a history or evidence of focal neurological symptoms or signs.

Initial assessment of patients with MS

Refer people suspected of having MS for diagnosis by a consultant neurologist or a specialist under their supervision.

Diagnosing patients with multiple sclerosis



In patients who show clinical and radiological findings suggestive of MS but do not fulfill McDonald diagnostic criteria, follow-up brain MRI is required:

- 3–6 months after the baseline scan is recommended in patients with CIS who have an abnormal baseline MRI scan but do not fulfil McDonald diagnostic criteria.
- If the second brain scan is inconclusive, a third can be acquired 6–12 months later.
- In patients with Radiological Isolated Syndrome (RIS), a follow-up brain scan 3–6 months after the initial MRI is also recommended.
- Follow-up spinal cord MRI in patients with Clinical Isolated Syndrome (CIS), to demon- strate DIS and DIT, seems to have limited value and should not be routinely performed.

In patients who have atypical clinical or MRI findings thorough investigations to identify MS mimickers need to be performed. Although CSF analysis is not required to establish the diagnosis of MS, it is recommended to obtain CSF in atypical presentations in order to

exclude other diseases, especially in pediatric patients. Atypical findings can be summarized as follows:

- Atypical clinical presentations such as bilateral optic neuritis, hyperacute myelitis with predominately motor involvement, seizures, extrapyramidal symptoms, or confusion may necessitate further appropriate workup.

Atypical MRI findings such as simultaneous enhancement of all lesions, persistent enhance- ment of the lesions for more than 6 months, lack of periventricular lesions, or a longitudi- nally extensive lesion in the spinal cord require more attention to exclude other diagnoses.

Managing patients with MS

Information & support for patients at time of diagnosis

The consultant neurologist should ensure that people with MS, and with their agreement their family members or carers, are offered oral and written information at the time of diag- nosis. This should include, but not be limited to, information about:

- What MS is
- Treatments, including disease-modifying therapies
- Symptom management
- How support groups, local services, social services and national charities are organized and how to get in touch with them
- Online resources

The consultant neurologist should advise the patient regarding:

- The involved risks of driving and the associated hazards
- His/her entitlement to use parking slots dedicated for people with determination

When applicable, discuss with the person with MS and their family members or carers whether they have social care needs and if so refer them to social services for assessment. Ensure the needs of children of people with MS are addressed.

Offer the person with MS a face-to-face follow-up appointment with a healthcare profes- sional with expertise in MS to take place within 6 weeks of diagnosis.

Ongoing information and support

Individuals diagnosed with MS should be advised to undergo a comprehensive annual care review. The frequency of these reviews should be altered to their specific conditions, deter- mining the necessary visit schedules and the comprehensive scope of care to be covered.

Review information, support and social care needs regularly. Continue to offer information and support to people with MS or their family members or carers even if this has been de- clined previously.

Ensure people with MS and their family members or carers have a management plan that includes who to contact if their symptoms change significantly

Explain to people with MS that the possible causes of symptom changes include:

- Another illness such as an infection
- Further relapse
- Change of disease status (for example progression)

Talk to people with MS and their family members or carers about the possibility that the condition might lead to cognitive problems. Provide ongoing information and support tailored to the person's changing needs or cir- cumstances, for example, when planning to have children, if their MS is changing to a more progressive phase or as their MS becomes more advanced.

Explain to carers (including young carers) about their right to a carer's assessment and tell them about other sources of information and support that may be available. Review information, support and social care needs regularly. Continue to offer information and support to people with MS or their family members or carers even if this has been de- clined previously.

Ensure people with MS and their family members or carers have a management plan that includes who to contact if their symptoms change significantly. Explain to people with MS that the possible causes of symptom changes include:

- Another illness such as an infection
- Further relapse
- Change of disease status (for example progression)

Talk to people with MS and their family members or carers about the possibility that the condition might lead to cognitive problems. Provide ongoing information and support tailored to the person's changing needs or cir- cumstances, for example, when planning to have children, if their MS is changing to a more progressive phase or as their MS becomes more advanced. Explain to carers (including young carers) about their right to a carer's assessment and tell them about other sources of information and support that may be available.

Information and support for people planning to have children or who are pregnant

Ask the person with MS soon after diagnosis and at regular intervals if they have any plans for starting or extending their family now or in the future, either through pregnancy or adoption.

Explain to people with MS that they should discuss with their healthcare professionals if they are planning to start or extend their family or become pregnant. In particular, ensure that people taking disease-modifying treatments understand that they should tell their healthcare professionals straight away if they are trying to become pregnant or if they be- come pregnant.

Explain to people with MS, and their partners if appropriate, that MS should not stop them from planning a family. Offer the opportunity to talk with a healthcare professional with knowledge of MS to answer any questions they have. For example, this may include discuss- ing the following:

- That fertility is not affected by MS.
- That pregnancy can be well managed in people with MS.
- The risk of the child developing MS.

- Taking vitamin D and folic acid supplements before and during pregnancy.
- Possible changes to medicine used before and during pregnancy.
- That pregnancy does not increase the risk of disease progression.
- That relapses may decrease during pregnancy and may increase 3 to 6 months after childbirth before returning to pre-pregnancy rates.
- That birth options and pain relief choices available (including epidurals) should not be affected by MS.
- That breastfeeding is safe unless the person with MS is taking certain disease-modify- ing treatments.
- Support that may be available with caring for and supporting children.
- Discuss caring for a child and the possible impact of MS symptoms, such as fatigue, and how these could be managed.

Information and support for people as MS becomes more advanced, including those approaching the end of their life

Give people with MS that is becoming more advanced and their family members or carers information and support covering:

- Social isolation and feelings of depression
- Mobility aids and home adaptations
- Other support available, such as legal rights including social care, employment rights and benefits, and the right to a carer's assessment.

Explain to people with advanced MS and their family members or carers about the services available (for example, occupational therapy, palliative care and social services) and give them support to access them if needed.

For advice on identifying people who may be approaching the end of their life and providing information and support, follow the recommendations in international guideline on end-of- life care for adults.

When appropriate, explain to the person with MS (and their family members or carers if the person wishes) about advance care planning and power of attorney. Think about discussing advance care planning early if you expect the person's ability to communicate, cognitive status or mental capacity will deteriorate. Follow the recommendations on advance care planning in international guideline on decision making and mental capacity.

Care coordination for patients with MS

Offer the person with MS an appropriate single point of contact among primary care pro- fessionals with knowledge of MS services to coordinate care and help them access services. Care for people with MS using a coordinated multidisciplinary approach. Involve profession- als who can best meet the needs of the person with MS and who have expertise in managing MS including:

- MS nurses
- Consultant neurologists
- Physiotherapists with expertise in MS and occupational therapists
  Speech and language therapists, psychologists, dietitians, social care, continence specialists and
- Consultants in rehabilitation medicine
- Primary healthcare team who shall be trained with knowledge of MS.

8. Azathioprine and Mycophenolate are unlicensed for MS and not first choices as MS DMT. But they do have varying levels of efficacy and may be treatment options when licensed DMT are unavailable or unaffordable
9. The traditional view of MS treatment has been one of caution i.e. using higher efficacy medications only when lower efficacy medications did not control the disease – the 'escalation' approach. Long-term safety concerns were the important reason for this approach. However, this approach has been criticized justifiably for the following reasons

    a. Benign RRMS MS is not truly benign in the majority of cases and can only be diag- nosed retrospectively.

    b. It is not always possible to predict reliably long-term outcomes at onset, although many clinical, radiological and laboratory factors have been shown to be predictive of long-term outcomes in individual patients.

    c. A significant number of patients will not achieve disease control and will switch to a high efficacy agent in time.

    d. Time lost is not regained.

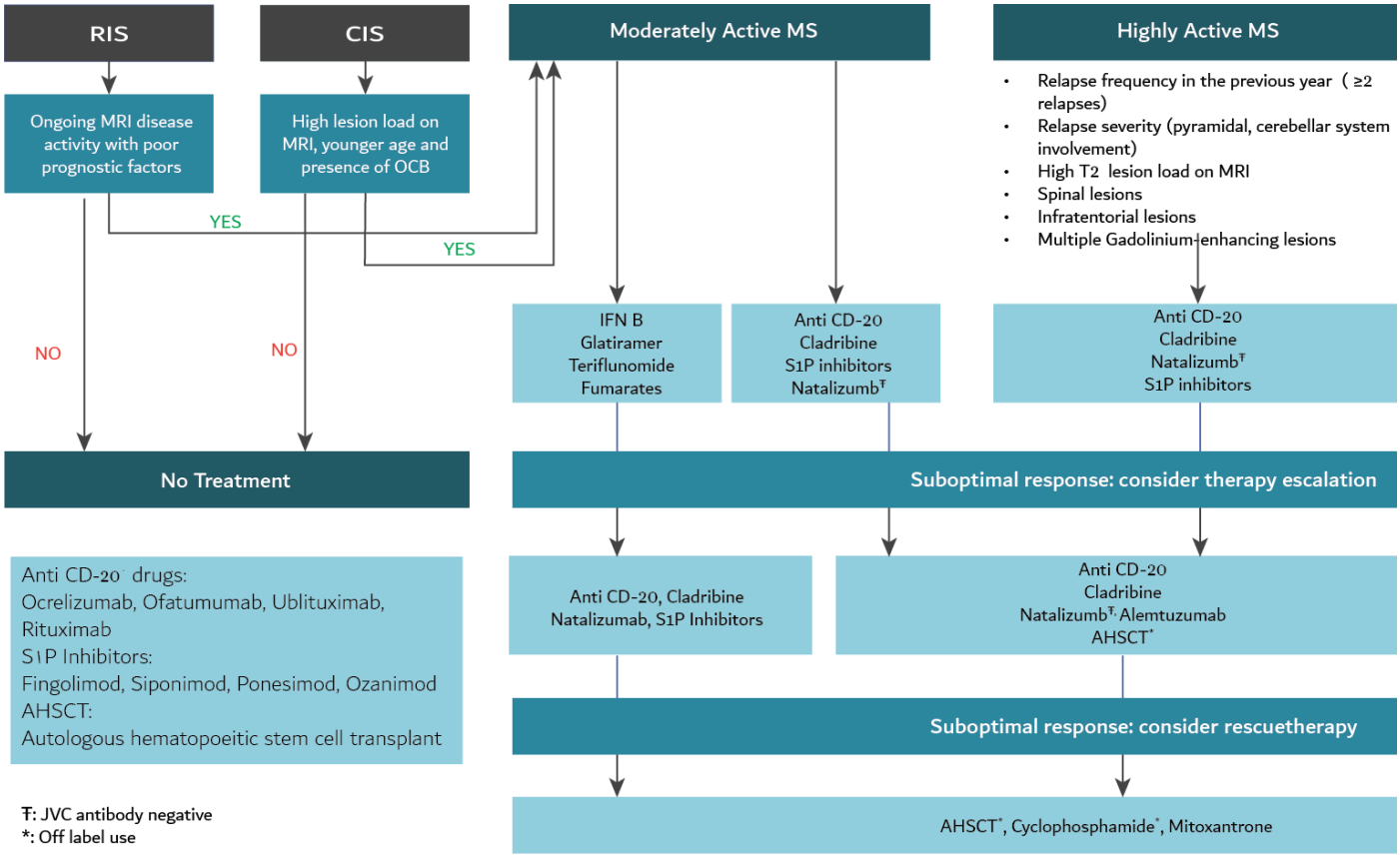
    e. Progression and disability accumulation happen earlier in those on lower efficacy medications.

    f. While the notion that "high efficacy DMTs cause more life-threatening side effects", was applicable in the era of cyclophosphamide, mitoxantrone and natalizumab (be- fore PML de-risking strategies), that is not true with the current DMT landscape. Even for those drugs with the potential for long term side effects, de-risking ap- proaches can effectively reduce harm e.g. JCV index monitoring and extended inter- val dosing for natalizumab.

    g. The induction approach of using higher efficacy drugs from the beginning is justi- fiable in many cases.

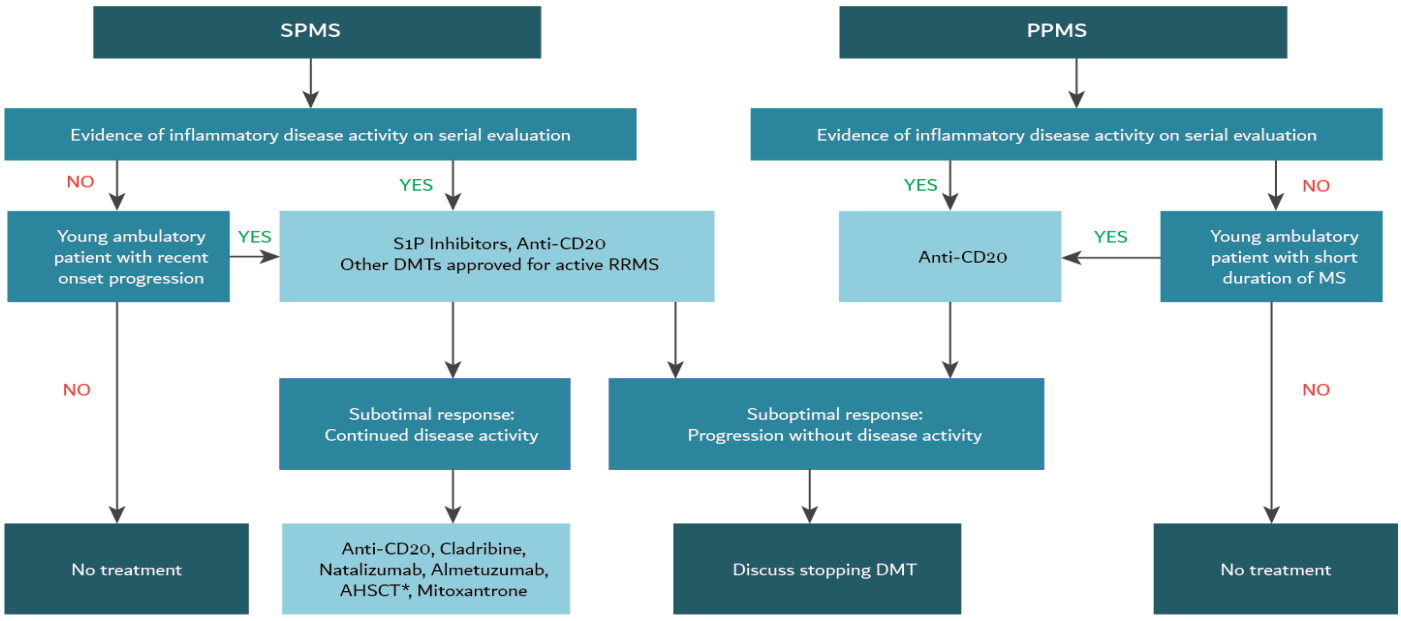
8. Defining MS stage and severity is helpful in deciding the drug of choice.
9. The goal of treatment with DMT is to achieve no evidence of disease activity status (NEDA) typically the absence of relapses, progression, and MRI changes.
10. Evidence of continued disease activity is a reason to switch treatment.
11. Pregnancy, breast feeding and MS in children have unique considerations.
12. Adherence to the recommended laboratory screening, as stipulated by the FDA or EMA, is imperative upon the initiation of each individual disease-modifying therapy. Subsequent screening, beyond the initial initiation, shall be determined at the sole discretion of the treating physician. Such decisions will be guided by their clinical evaluation of the patient's condition.

Treatment algorithm for RIS, CIS and RRMS



₸: JVC antibody negative
*: Off label use

Treatment algorithm for PPMS and SPMS



Anti CD-20 drugs:
Ocrelizumab, Ofatumumab, Ublituximab, Rituximab
S1P Inhibitors:
Fingolimod, Siponimod, Ponesimod, Ozanimod
AHSCT:
Autologous hematopoeitic stem cell transplant

Treatment of multiple sclerosis during pregnancy and breastfeeding

1. Women are generally advised to consider pregnancy after at least 1 year of disease remission irrespective of the DMT used.
2. Patients on IFNB, GA, DMF, and Natalizumab can continue their DMTs till conception is confirmed.
3. IFNB and GA can be continued during pregnancy.
4. In highly active patients, natalizumab may be continued until 34 weeks of gestation to minimize the risk of disease reactivation, preferably with an extended interval dosing.
5. The following DMTs require washout periods:
    a. at least two months for fingolimod,
    b. 7 days for Ponesimod,
    c. 10 days for Siponimod
    d. 4 and 6 months after the last course of alemtuzumab and cladribine, respectively.
    e. For teriflunomide, it is recommended to perform the accelerated elimination pro- cedure.
    f. Patients on ocrelizumab, Ublituximab or rituximab can attempt conception in the menstrual cycle following the last injection
    g. Patients on ofatumumab can continue treatment until conception.
    h. DMF can be continued till conception
6. Patients on alemtuzumab should test for thyroid function monthly during pregnancy.
7. Patients on DMF or Teriflunomide can be switched to GA or IFNB during pregnancy
8. Patients on S1P modulators can be switched to Natalizumab, Ocrelizumab or Rituximab
9. Monitoring B cells counts during pregnancy may help stratify risk of relapse.
10. Advice all women of childbearing potential that DMDs are not licensed during pregnancy, except glatiramer acetate 20mg/ml.
11. Intravenous corticosteroids are probably safe to treat relapses during pregnancy while the data for plasmapheresis is limited.
12. Breastfeeding is recommended for women on IFNB, GA, natalizumab, B-cell depleting therapies and alemtuzumab. For monoclonal antibodies, breastfeeding should be initiated at least one-week post-partum and 4 hours after infusion. Breastfeeding should be avoided in women on oral therapies including teriflunomide, S1P receptor modulators, cladribine and DMF.

Treatment of pediatric multiple sclerosis

All children with active MS are recommended to initiate treatment with DMF, Fingolimod or Teriflunomide. However, off label use of other high efficacy DMT can be justified in the presence of ongoing clinical or radiological disease activity with the above first line agents following general principles used in adults or with highly active disease.

Autologous haemopoeitic stem cells transplantation (AHSCT)

Consider offering AHSCT to:

- Patients with rapidly evolving aggressive MS and suboptimal response to one of the high efficacy medications
- Patients with highly active disease and suboptimal response to at least 2 high efficacy DMTs (third line rescue therapy)
- Pattients with progressive Multiple sclerosis (SPMS or PPMS) in the setting of active inflammation, either clinically or radiologically, and not responding to DMTs.

The selected patients should preferably be below the age of 50 years with EDSS ≤ 5.5 (am- bulating independently) and disease duration less than 10 years

Monitoring treatment response

1. Consider combining MRI with clinical measures when evaluating disease evolution in treated patients.
2. Clinicians should monitor MRI disease activity from the clinical onset of disease to detect the accumulation of new lesions in order to inform treatment decisions in people with MS using DMTs.
3. Clinicians should recognize that relapses or new MRI detected lesions may develop after initiation of a DMT and before the treatment becomes effective in people with MS who are using DMTs.
4. When monitoring treatment response in patients treated with DMDs, perform a standardized reference brain MRI usually within 6 months of treatment onset and compare it with a further brain MRI performed typically 12 months after starting treatment. Adjust the timing of both MRIs, considering the following aspects:
    a. The drug's mechanism of action (particularly the speed of action)
    b. Disease activity (including clinical and MRI measures).
5. When monitoring treatment response in patients treated with DMDs, the measurement of new or unequivocally enlarging T2 lesions is the preferred MRI method supplemented by GAD-enhancing lesions for monitoring treatment response. Evaluation of these parameters requires the following:
    1. High-quality, standardized MRI scans.
    2. Interpretation by highly qualified readers with experience in MS.
    3. When monitoring for progressive multifocal leukoencephalopathy (PML) in patients treated with DMDs,
    4. Perform a standardized reference brain MRI: every year in low-risk PML patients.
    5. More frequent MRIs (on a 3–6monthly basis) in high-risk PML patients (John Cun- ningham virus (JCV) positive, natalizumab treatment duration over 18months).
    6. In patients with high risk of PML who switch drugs at the time that the current treatment is; discontinued and after the new treatment is started.
6. Clinicians should monitor the reproductive plans of women with MS and counsel regarding reproductive risks and use of birth control during DMT use in women of child- bearing potential who have MS.

Treating patients with suboptimal response

1. Clinicians should monitor for medication adherence, AEs, tolerability, safety, and effectiveness of the therapy in people with MS on DMTs.
2. Clinicians should follow up every 6-12 months or according to medication-specific REMS in people with MS on DMTs.
3. Suboptimal response on continuous DMTs should be considered after 1 year of treatment in patients with ≥ 1 relapse and/or disability progression or ≥ 2 active MRI le- sions (Gd+ and/or new T2W), using as baseline an MRI performed 6 months after treatment initiation. In patients on IRT, breakthrough disease should be assessed at least 18 months after treatment initiation.
4. In patients with moderately active disease and suboptimal response to first-line therapies as defined above, treatment escalation to S1PR modulators, natalizumab, B cell depleting therapies or cladribine should be considered.
5. It is recommended to have a reference MRI 6 months after treatment initiation for comparison (re-baseline MRI).
6. In patients with HDA and suboptimal response to DMTs, treatment escalation to natalizumab, B cell depleting therapies cladribine or alemtuzumab should be considered
7. In patients with READ and suboptimal response to the initial DMT, a lateral shift among alemtuzumab, B cell depleting therapies and natalizumab or AHSCT should be considered. The choice among them should be based on risk stratification including serum anti-JCV antibody, prior immunosuppressant use and comorbidities.
8. In patients on alemtuzumab fulfilling criteria for suboptimal response beyond the first 2 years of treatment, a third course of DMT is recommended before shifting to another therapy. In patients on cladribine, with suboptimal response in the third and fourth year of treatment, a third , and possibly fourth, course of cladribine may be adminis- tered or shifting to one of the monoclonal antibodies. Beyond the fourth year, and in case of suboptimal response it is recommended to administer a third course keeping in mind that data supporting such approach with cladribine is still limited.
9. Rituximab can be used off label for all levels of activity in special populations such as refugees, or in countries where other appropriate options are either unavailable or unaffordable.
10. In patients with evidence of breakthrough disease on any of the second line medications, a lateral switch based on the risk stratification strategy mentioned above or AHSCT should be considered before resorting to third line therapies including cyclophosphamide or mitoxantrone.

Modifying risk factors

1. Encourage people with MS to exercise. Advise them that regular exercise may have
2. beneficial effects on their MS and does not have any harmful effects on their MS.
3. Advise people with MS not to smoke and explain that it will increase the progression of disability.
4. Offer vaccinations in line with the recently published ECTRIMS guidelines on vaccination in MS patients below

Vaccine	Type	Schedule	Indications		
			General population	Special population	
Seasonal influenza	Inactivated Fractioned or subunits	Single IM/SC dose every year	Annually, especially in vase of present/future IS and/or significant disability	*A* *B* *C*	During any trimerster Annually for all From 6m, in case of present/future IS
Pneumococcal: 13-PCV, 23-PPV, 20-PCV	Inactivated	13-PCV and 23-PPV (at least 2 months apart) OR Single dose 20-PCV	In case of pre-sent/future immuno-suppression and/or sig-nificant disability[a]	*C*	PCV13 as age-appropriate and PPSV23 2 months apart, in case of present/future IS
Tetanus- Diphtheria (dT) Tetanus- diphtheria pertussis (dTap)	Inactivated Tetanus and diphtheria toxoids	3 IM doses (0,1, 6 months) in naïve patients Single IM booster dose in first vaccinated	Same indications as in the general population[b]	*A*	dTap during the end of the second or the third trimester. Repeat during each pregnancy[c]
Measles, mumps, rubella (MMR)	Live attenuated	2 IM/SC doses given 4 weeks apart	Recommended in seronegative patients Complete 4 weeks before immunosuppression[d]	*A*	In seronegative, vaccinate in the postpartum period before initiating DMT.
Varicella	Live attenuated	2 IM/SC doses given 4 weeks apart	Recommended in seronegative patients. Complete 4 weeks before immunosuppression[d]	*A*	In seronegative, vaccinate in the postpartum period before initiating DMT.
Human papillomavirus	Inactivated (recombinant)	3 IM doses at months 0, 2, and 6	Consider in women and men with MS who will receive treatment with ALZ, S1P modulators, CLAD or anti- CD20 drugs, independently of their age[e]	*C*	Ensure complete immunization in all girls and boys[b]

Herpes zoster	Inactivated (re-combi-nant)	2 IM doses se-pa-rated by 2–6 months	Consider in patients aged over 18 years g if treatment with CLAD, ALZ, S1P modulator, NTZ, and anti- CD20 drugs	*B* *C*	Especially indi-cat-ed in those receiving immuno-suppressive thera-pies From 18 years of age
COVID-19	mRNA Ade-noviral vector Inactivated (recombinant adyuvanted)	Vaccination with one or two-dose scheme[j] Additional booster doses[k]	Recommended for all MS patients	*A* *C*	During any trimes-ter mRNA vaccines, from 6 months of age, in case of pres-ent/future IS
Hepatitis B	Inactivated (re-combinant)	Regular vaccines 3 IM doses at months 0,1,6 Enhanced im-munity vaccines h 4 IM doses (0,1,2,6- 12 months) for high load (40mcg) or ad-juvanted (AS03) 2 IM doses (0,1 months) for ad-juvanted (CpG 1018)	Consider in high-risk[i] seronegative patients, especially if treatment with anti-CD20 thera-pies	*C*	Ensure complete immunization in all girls and boys[b]

A Pregnant patients

B Patients of 60 years and older

C Patients under 18 years of age.

a 13-valent pneumococcal conjugate vaccine (13-PCV, Prevenar 13®); 20-valent pneumococcal conjugate vaccine (20-PCV, Appen-xnar®) Pneumococcal polysac-charide vaccine (PPSV23, Pnaumovax®). Use following general recommendations for immunosup-pression. Age and/or comorbidities should also be considered in the indication of pneumococcal vaccination following guidelines applicable in each country. For children: routine vaccination with PCV13 as age- appropriate and in children of at least 2 years of age administer PPSV23 2 months apart.

b Following national immunization schedules.

c Unless national recommendations state otherwise.

d Always avoid in MS patients who are already receiving the following immunosuppressive therapies (sphingosine-1-phosphate (S1 P) modulators, anti-CD20 monoclonal antibodies and before immune restoration for cladribine and alemtuzumab). Ideally avoid in MS patients who are already receiving the following immunosuppressive therapies (natalizumab, DMF and teriflunomide with-out lymphopenia). In these patients and in very exceptional cases, such as high risk of infection, vaccination with live attenuated vaccines could be considered if the potential risk of acquiring the infection is superior to the risk of developing vaccine-related infections.

e There can be limitations and variations regarding upper age limit depending on the country and the Summary of product charac-teristics.

f A live, attenuated herpes zoster vaccine (Zostavax®) is also available, but not recommended for patients who are receiving immu-nosuppressants.

g With a background of chickenpox disease or live-attenuated varicella vaccination (otherwise consider varicella immunization).

h Enhanced Immunity Vaccines include High load (HBVaxpro® 40mcg) or adjuvanted (AS03-Fendrix®, CpG 1018-Heplisav®). Con-sider If onset of immunosup-pressants in the following 6 months or in patients already immunosuppressed.

i Risk of sexual exposure, patients on dialysis, parenteral drug users, healthcare workers with occupational risk, and patients with specific comorbidities (HIV or HCV infection, chronic liver or kidney disease, solid organ transplant/hemopoietic stem cell trans-plantation recipients and/or people receiving blood products.

j EMA authorized COVID-19 vaccines: Comirnaty (0, 28 days), Spikevax (0, 28 days) Valneva (0,28 days), Nuvaxoid (0,21 days), Vaxzevria (0, 28 days), Jcovden (single-dose), VidPrevtyn Beta (single booster after mRNA) Available at: https://www.ema.europa.eu/en/human-regulatory/overview/public-health- threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-authorised#originally-authorised-covid-19-vaccines-section.

k Follow most updated local/country guidance on COVID-19 vaccination for high-risk patients.

IS immunosuppression

Symptomatic treatment of MS

Fatigue

1. Ask people with MS if they are experiencing fatigue, sudden tiredness or a change in their energy levels affecting their daily living.
2. Do not assume that the person's fatigue is always caused by MS. Assess for other causes and manage these or refer the person for management if indicated. Other causes of fatigue may include:
    a. Sleep problems
    b. Symptoms of MS, such as pain, spasticity and bladder dysfunction
    c. Side effects of medicines
    d. Illnesses, such as infections, anemia and thyroid dysfunction
    e. Anxiety and depression.
3. Explain that MS-related fatigue may be brought on by heat or biological, physical and emotional stress.
4. Offer people with MS and fatigue a personalized discussion about how they can be supported to self-manage their fatigue. This could include:
    a. Identifying goals and priorities
    b. Advice on conserving their energy
    c. Reviewing lifestyle factors such as diet and exercise
    d. Using stress management and wellbeing approaches such as mindfulness and cognitive behavioral techniques to help with day-to-day activities.
5. Advise people that aerobic, resistive and balance exercises, including yoga and Pilates, may be helpful in treating MS-related fatigue.
6. Explain to people that there is no evidence that a specific diet will improve fatigue in people with MS, but that a healthy diet will benefit their general health.
7. For people with MS with moderately impaired mobility (an EDSS [Expanded Disability Status Scale] score of greater than or equal to 4), consider a combination of:
    a. A program of supervised aerobic and moderate progressive resistance activity and
    b. Cognitive behavioral techniques.
8. Do not use vitamin B12 injections to treat fatigue in people with MS.
9. Do not offer hyperbaric oxygen to treat fatigue in people with MS.
10. Use shared decision making to decide whether to try a medicine for fatigue and which would be most suitable. Taking into account the needs, priorities and preferences of the person with MS, and the risks and benefits of each treatment, consider any of the following:
    a. Amantadine
    b. Modafinil, except in people who are pregnant or planning pregnancy: use the lowest effective dose

c. Selective serotonin reuptake inhibitor (SSRI): use the lowest dose recommended for licensed indications

11. Regularly review treatment to monitor effectiveness, safety and acceptability, adjust the dose, and decide whether to continue or stop the medicine.

Mobility problems

1. Ensure people with MS and mobility problems have access to an assessment to establish individual goals and discuss ways to achieve them. This would usually involve rehabilitation specialists and physiotherapists with expertise in MS.
2. Consider vestibular rehabilitation for people with MS who have fatigue or mobility problems associated with limited standing balance.
3. Consider supervised exercise programs involving moderate progressive resistance training and aerobic exercise to treat people with MS who have mobility problems or fatigue.
4. Consider fampridine in patients with impaired mobility who are still ambulatory
5. Help the person with MS continue to exercise, for example, by referring them to a physiotherapist with expertise in MS or to exercise referral schemes.

Spasticity

1. Suspect spasticity when a person with MS presents with any of the following:
   a. Involuntary muscle movements (spasms)
   b. Muscle stiffness
   c. Pain and restriction with certain movements or positions causing difficulty in performing various activities
   d. A change in their mobility or upper limb function.
2. Assess people with MS and suspected spasticity for factors that might worsen spasticity, for example, pressure ulcers, bladder and bowel dysfunction and infections, poor posture or positioning, and pain. Provide support and information to help people with MS, and their families and carers if appropriate, to prevent and manage these factors.
3. Discuss with the person the balance between the benefits and harms of treating spasticity. In particular, explain that some people use their spasticity to maintain their posture and ability to stand, walk or transfer, and that treatment with muscle relaxants may adversely affect this.
4. Consider oral baclofen or tinazidine as a first-line drug treatment to treat spasticity in people with MS who have specific treatment goals such as improving mobility or easing pain and discomfort. Take into account any contraindications, comorbidities and the person's preferences.
5. If oral baclofen or tinazidine are not tolerated or does not provide adequate relief, consider gabapentin as a second-line option to treat spasticity in people with MS.
6. When using oral baclofen, tinazidine or gabapentin to treat spasticity in people with MS, explain to the person that they should:
   a. Increase the dose gradually in at least 2-week increments to optimize symptom improvement or until they reach the maximum dose they can tolerate
   b. Stop taking the medicine if there is no benefit at the maximum tolerated dose (ex- plain that baclofen can cause harm if stopped suddenly and that special precautions may be needed when stopping specific medicines)
   c. Have their medicines reviewed at least annually once the optimal dose has been reached.

7. Consider a combination of oral baclofen or tinazidine with gabapentin for people with MS if:
   a. Individual medicines do not provide adequate relief or
   b. Side effects from individual medicines prevent the dose being increased.
8. If spasticity is causing significant impairments in mobility, posture or function and initial treatments are unsuccessful, refer to a multidisciplinary team experienced in the management of spasticity for assessment and treatment planning.

Oscillopsia

1. Consider gabapentin as a first-line drug to treat oscillopsia in people with MS.
2. Consider memantine as the second-line treatment for oscillopsia in people with MS.
3. Refer the person with MS for specialist advice if there is no improvement in oscillopsia after treatment with gabapentin and memantine or if side effects prevent continued use.

Depression and anxiety

Consider antidepressants to treat depression in people with MS.

Pain

1. Assess and investigate the cause of pain to establish a diagnosis and offer treatment specific to the cause of the pain.
2. Be mindful of the impact of pain on the mental wellbeing of people with MS, and provide advice and support.
3. Be aware that musculoskeletal pain is common in people with MS and is usually secondary to problems with immobility, spasticity and posture. Assess musculoskeletal pain and offer treatment appropriate to the cause.
4. Consider gabapentin, duloxetin or pregabalin in patients with central neuropathic pain

Cognitive and memory problems

1. Be aware that the symptoms of MS can include cognitive problems, including memory problems, that the person may not immediately recognize or associate with their MS.
2. Assess cognition as part of the person's comprehensive review. Tailor the assessment to the person's needs, for example, use a clinic interview or brief formal assessment, or consider referral for a full neuropsychological assessment if needed.
3. Be aware that anxiety, depression, difficulty sleeping, fatigue and medication can affect cognition. Assess for and offer management appropriate for these issues in people with MS and cognitive or memory problems.
4. Consider referring people with MS and persisting cognitive impairments to an occupational therapist and/or a neuropsychologist to assess and manage these symptoms according to the person's needs.

Health Outcomes Indicators

Percentage of patients meeting the NEDA-3 criteria

Description title	Percentage of patients meeting the NEDA-3 criteria
Definition	Percentage of patients meeting the three-dimensional NEDA criteria out of the total patients diagnosed with MS

Numerator	Number of patients showing:
	• No clinical relapses +
	• No confirmed EDSS progression sustained for 6 months
	  • If baseline EDSS 0, EDSS increase <1.5 points
	  • If baseline EDSS ≥1, EDSS increase <1 point
	  • If baseline EDSS >5, EDSS increase <0.5 points
	• No new T1 gadolinium-enhanced lesions +
	• No new or newly enlarging T2 lesions

Denominator	Total number of patients diagnosed with MS
Exclusion criteria	Patients not meeting the NEDA-3 criteria
Unit of measure	Percentage (Numerator/Denominator x 100)
Measure target and/or threshold	Higher percentage of patients is better
Rationale	NEDA serves as a treatment goal in MS management. The ul- timate aim of MS treatment is to prevent disease progression and disability while maintaining quality of life. NEDA provides a clear target for clinicians and patients to strive for.

Percentage of patients meeting the NEDA-4 criteria

Description title	Percentage of patients meeting the NEDA-4 criteria
Definition	Percentage of patients meeting the four-dimensional NEDA criteria out of the total patients diagnosed with MS
Numerator	Number of patients showing: • NEDA-3 criteria shown above + • Annualized whole brain volume loss less than 0.4%
Denominator	Total number of patients diagnosed with MS
Exclusion criteria	Patients not meeting the NEDA-4 criteria
Unit of measure	Percentage (Numerator/Denominator x 100)
Measure target and/or threshold	Higher percentage of patients is better
Rationale	NEDA serves as a treatment goal in MS management. The ul- timate aim of MS treatment is to prevent disease progression and disability while maintaining quality of life. NEDA provides a clear target for clinicians and patients to strive for.

Baseline EDSS score in MS patients

Description title	Baseline EDSS
Definition	Percentage of patients showing no or minimal disability at the time of diagnosis out of the total number of patients diag- nosed with MS
Numerator	Number of patients with baseline EDSS ≤2.0
Denominator	Total number of patients diagnosed with MS
Exclusion criteria	EDSS measured at subsequent assessment encounters after diagnosis
Unit of measure	Percentage (Numerator/Denominator x 100)
Measure target and/or threshold	Higher percentage of patients is better
Rationale	The Expanded Disability Status Scale (EDSS) is a method of quantifying disability in multiple sclerosis and monitoring changes in the level of disability over time. While the EDSS does not directly measure the time to diagnosis of MS, it can indirectly reflect the duration of disease progression since di- agnosis. Patients with a longer duration of MS are more likely to have accumulated disability and higher EDSS scores, indi- cating greater functional impairment.

Time to diagnosis for MS

Description title	Time to diagnosis
Definition	The percentage of patients with suggestive symptoms of MS and were confirmed as MS patients within 6 months from the initial symptom.
Numerator	Number of patients diagnosed with MS in ≤6 months
Denominator	Total number of patients diagnosed with MS
Exclusion criteria	Patients with diagnosis of another neuromuscular disorder mimicking MS
Unit of measure	Percentage (Numerator/Denominator x 100)
Measure target and/or threshold	Higher percentage of patients is better
Rationale	Research has shown that the early use of DMTs can signifi- cantly slow the disease's progression, reduce the frequency and severity of relapses, and limit new disease activity as seen on MRI scans. Starting treatment early in the disease course can prevent or delay the accumulation of disability, potentially altering the disease's trajectory in a positive way. Early diag- nosis and treatment can help protect the nervous system from damage by reducing inflammation and the formation of new lesions. This preservation of neurological function is essential for maintaining mobility, cognitive function, and independence for as long as possible.

Relapse rates of MS patients per class of DMT patients

Description title	Relapse Rate
Definition	Number of relapses per class of DMT per patient per year
Numerator	Number of relapses per patient per class of DMT
Denominator	Total number of patients diagnosed with MS
Exclusion criteria	Patients not recieving DMTs
Unit of measure	Frequency distribution of number of relapses per class of DMT
Measure target and/or threshold	Higher frequency indicates poor quality
Rationale	This KPI measures the frequency of relapses, which are ep- isodes of new or worsening neurological symptoms. A lower relapse rate indicates better disease control, making this an essential KPI for evaluating the efficacy of DMTs in relapsing forms of MS.

MRI Progression of patients diagnosed with MS

Description title	MRI progression
Definition	Number of patients with new T1 gadolinium-enhanced lesions or new or enlarged T2 gadolinium-enhanced lesions out of the total number of patients diagnosed with MS
Numerator	Number of patients developing new T1 gadolinium-enhanced lesions and/or new or enlared T2 gadolinium-enhanced lesions over a period of 6 months
Denominator	Total number of patients diagnosed with MS
Exclusion criteria	Patient not diagnosed with MS
Unit of measure	Percentage (Numerator/Denominator x 100)
Measure target and/or threshold	Higher percentage indicates a poor quality
Rationale	Magnetic resonance imaging (MRI) is a critical tool in MS for detecting lesions in the brain and spinal cord. This KPI focuses on the number and volume of lesions, providing insight into disease activity and the effectiveness of DMTs in reducing in- flammatory activity.

MRI monitoring for patients with MS

Description title	MRI monitoring for patients with MS
Definition	Percentage of patients who had a brain MRI scan in the last 24 months and care management decisions updated.
Numerator	Patients who had a brain MRI scan in the last 24 months and care management decisions updated. Definition: Care management decisions updated defined as re-affirmation or adjustment to the treatment plan, adjustment or initiation of appropriate medication, or further testing.
Denominator	Total number of patients diagnosed with MS
Exclusion criteria	• Patient declines referral to MRI in the last 24 months • MRI not clinically indicated given patient circumstances on date of encounter • Patient unable to have an MRI and this reason docu- mented during measurement period
Unit of measure	Percentage (Numerator/Denominator x 100)
Measure target and/or threshold	Higher percentage indicates a better quality
Rationale	Magnetic resonance imaging (MRI) is a critical tool in MS for detecting lesions in the brain and spinal cord.

Bladder, Bowel, and Sexual Dysfunction Screening and Follow Up for Patients with MS

Description title	Bladder, Bowel, and Sexual Dysfunction Screening and Fol- low-Up for Patients with MS
Definition	Percentage of patients with MS who were screened for at least one of three symptoms: bladder, bowel, or sexual dysfunction in the past 12 months, and if screening positive for any one of these symptoms had appropriate follow-up care.
Numerator	Patients with MS who were screened for at least one of three symptoms: bladder, bowel, or sexual dysfunction in the past 12 months, and if screening positive had appropriate follow-up care. Definitions: • Screened is defined as an assessment of symptoms. • Appropriate follow-up is defined as adjustment to the treatment plan, adjustment or initiation of appropri- ate medication, further testing, counseling on lifestyle changes, or referral to an appropriate healthcare provid- er.
Denominator	Total number of patients diagnosed with MS
Exclusion criteria	Patient refuses or patient declines on date of encounter
Unit of measure	Percentage (Numerator/Denominator x 100)
Measure target and/or threshold	Higher percentage indicates a better quality
Rationale	Bladder, bowel, and sexual dysfunction are common and im- pactful symptoms for patients with Multiple Sclerosis (MS), a chronic autoimmune disease of the central nervous system. These symptoms can significantly affect the quality of life, emotional well-being, and social and occupational functioning of individuals with MS. Screening and follow-up for these dys- functions are essential components of comprehensive MS care

Cognitive Impairment Screening and Follow-Up for Patients with MS

Description title	Cognitive Impairment Screening and Follow-Up for Patients with MS
Definition	Percentage of patients with MS who were screened* for cog- nitive impairment in the past 12 months and if screening pos- itive, patient was referred appropriately for further evaluation and management.
Numerator	Patients with MS were screened* for cognitive impairment in past 12 months, and if screening positive, patient was referred appropriately for further evaluation and management**. Definitions: *Screened is defined as administering any one of the following tools: • Brief International Assessment of Cognition for MS (BI- CAMS), • Symbol Digit Modalities Test (SDMT), • MS Neuropsychological Screening Questionnaire (MSNQ) Observer version, • Computerized Speed Cognitive Test (CST), • Processing Speed Test (PST), • Verbal fluency (phonemic and semantic), • Paced Auditory Serial Addition Test (PASAT),Rao Brief Repeatable Neuropsychological Battery (BRNB), • Minimal Assessment of Cognitive Function in MS (MACFIMS), • PROMIS, or • Montreal Cognitive Assessment (MoCA). **Further evaluation and management is defined as referral to: • MS neuropsychological rehabilitation • Neuropsychologist or psychologist, • Speech/language pathologist, or • Occupational therapist. Neuropsychological evaluation in the past 12 months, may be used to meet the numerator for screening and evaluation and management.
Denominator	Total number of patients diagnosed with MS
Exclusion criteria	• Patient declines to complete a cognitive assessment on date of encounter. • Patient is not able to complete a cognitive assessment on date of encounter. • Patient currently receiving treatment to address cogni- tive impairment.
Unit of measure	Percentage (Numerator/Denominator x 100)
Measure target and/or threshold	Higher percentage indicates a better quality
Rationale	Cognitive impairment is a common symptom in patients with Multiple Sclerosis (MS), affecting up to 70% of individuals over the course of their disease. Cognitive dysfunction can vary greatly among patients, both in terms of severity and the cog- nitive domains affected, which may include memory, attention, processing speed, executive functions, and verbal fluency. The significance of cognitive impairment screening and follow-up in MS patients lies in its profound impact on daily functioning, employment, social relationships, and overall quality of life.

Fatigue Screening and Follow-Up for Patients with MS

Description title	Fatigue Screening and Follow-Up for Patients with MS
Definition	Percentage of patients 18 years and older with diagnosis of MS who were screened for fatigue in past 12 months, and if screening positive were provided appropriate follow-up.
Numerator	Patients with MS who were screened* for fatigue in past 12 months, and if screening positive were provided appropriate follow-up.** Definitions *Screened is defined as use of one of the following validated fatigue rating instruments: • The Fatigue Severity Scale (FSS) or • Modified Fatigue Impact Scale or • Shortened Modified Fatigue Impact Scale **Follow-up for this measure is defined as adjustment to the treatment plan, adjustment or initiation of appropriate med- ication, further testing, referral to PT/OT, exercise program, lifestyle modification program, or referral to an appropriate healthcare provider.
Denominator	Total number of patients diagnosed with MS
Exclusion criteria	• Patients unable to complete a fatigue screening on date of encounter • Patient declines to complete a fatigue screening on date of encounter
Unit of measure	Percentage (Numerator/Denominator x 100)
Measure target and/or threshold	Higher percentage indicates a better quality
Rationale	Fatigue is one of the most common and debilitating symptoms reported by patients with Multiple Sclerosis (MS), affecting up to 80% of individuals at some point during the course of the disease. It can be profound, significantly interfering with daily activities, employment, and overall quality of life.

For any inquiries and additional information contact: EJADAH team on (Ejadah-DHIC@dha.gov.ae)