**MULTIPLE SCLEROSIS GUIDELINES: DISEASE-MODIFYING THERAPY**

**MUST**
- Ascertain, incorporate, and review preferences in terms of safety, route of administration, lifestyle, cost, efficacy, common adverse effects (AEs), and tolerability in the choice of DMT.
- Engage in an ongoing dialogue regarding treatment decisions throughout the disease course.
- Counsel those on DMTs to notify clinicians of new or worsening symptoms.

**SHOULD**
- Counsel patients with newly diagnosed MS about specific treatment options with DMTs at a dedicated treatment visit.
- Counsel that DMTs are prescribed to reduce relapses and new MRI lesion activity, and not prescribed for symptom improvement.
- Evaluate readiness or reluctance to initiate DMT and counsel on its importance.
- Counsel about comorbid disease, adverse health behaviors, and potential interactions of the DMT with concomitant medications.
- Evaluate barriers to treatment adherence and counsel on the importance of adherence.
- Discuss the benefits and risks of DMTs for patients with a single clinical demyelinating event with ≥2 brain lesions that have imaging characteristics consistent with MS, and then prescribe DMTs to those who decide they want this therapy.
- Offer DMTs to patients with relapsing forms of MS with recent clinical relapses or MRI activity.
- Review for medication adherence, AEs, tolerability, safety, and effectiveness of therapy and follow up either annually or according to medication-specific REMS.
- Monitor the reproductive plans of women with MS and counsel regarding reproductive risks and use of birth control during DMT use in women of childbearing potential.
- Counsel men with MS on their reproductive plans regarding treatment implications before initiating treatment with teriflunomide or cyclophosphamide.
- Do not prescribe mitoxantrone to patients with MS unless the potential benefits greatly outweigh the risks (high frequency of severe AEs).
- Prescribe alem替nuzumab, fingolimod, or natalizumab for patients with highly active MS.
- Offer ocrelizumab to patients with PPMS who are likely to benefit from this therapy unless risks of treatment outweigh the benefits.

**MAY**
- Recommend serial imaging at least annually for the first 5yrs and close follow-up rather than initiating DMT in patients with CIS or relapsing forms of MS who are not on DMT, have not had relapses in the preceding 2yrs, and do not have active new MRI lesion activity on recent imaging.
- Direct candidates for DMTs to support programs.
- Recommend azathioprine or cladribine for patients with relapsing forms of MS who do not have access to approved DMTs.
- Initiate natalizumab in patients with positive anti-JCV antibody index >0.9 only when there is a reasonable chance of benefit vs the risk of PML.

**Switching DMTs**
Counsel those considering natalizumab discontinuation about the increased risk of MS relapse or MRI-detected disease activity within 6mos of discontinuation.

**Monitoring**
- Monitor MRI disease activity from the clinical onset of disease to detect the accumulation of new lesions in order to inform treatment decisions.
- Recognize that relapses or new MRI-detected lesions may develop after initiation of a DMT and before the treatment becomes effective.
- Discuss switching DMTs in patients who have been using a DMT long enough for the treatment to take full effect and are adherent to their therapy when they experience ≥1 relapses, ≥2 unequivocally new MRI-detected lesions, or increased disability on examination, over a 1-yr period.
- Evaluate the degree of disease activity, adherence, AE profiles, and mechanism of action of DMTs when switching therapy in patients with breakthrough disease activity during DMT use.
- Discuss a change to non-injectable or less frequently injected DMTs in patients who report intolerable discomfort with the injections or in those who report injection fatigue.
- Inquire about medication AEs and attempt to manage these; then discuss a medication switch with patients for whom these AEs negatively influence adherence.
- Monitor laboratory abnormalities found on routine laboratory surveillance and discuss switching DMT or reducing dosage or frequency when there are persistent abnormalities.
- Counsel patients considering natalizumab, fingolimod, rituximab, ocrelizumab, and dimethyl fumarate about drug-associated PML risk.
- Discuss switching to a DMT with a lower PML risk with patients taking natalizumab who are or become JCV antibody-positive, especially with an index of >0.9 while on therapy.
- Counsel that new DMTs without long-term safety data have an undefined risk of malignancy and infection for patients starting or using new DMTs.
- Promptly discuss switching to an alternate DMT (especially for those using azathioprine, methotrexate, mycophenolate, cyclophosphamide, fingolimod, teriflunomide, alemtuzumab, or dimethyl fumarate) if a patient develops a malignancy.
- Switch DMTs if a patient develops a serious infection potentially linked to their DMT (does not pertain to PML management).
- Check for natalizumab antibodies in patients with infusion reactions before subsequent infusions, or in patients who experience breakthrough disease activity with natalizumab use; switch DMTs in patients with persistent natalizumab antibodies.
- When choosing to switch from natalizumab to fingolimod, initiate treatment within 8-12wks after natalizumab discontinuation (for reasons other than pregnancy or pregnancy planning) to diminish the return of disease activity.
- Counsel women to stop their DMT before conception for planned pregnancies, discontinue the DMT during pregnancy, and not to initiate DMTs during pregnancy unless the risk of MS activity during pregnancy outweighs the risk of DMT use.

**Stopping DMTs**
- Counsel patients with RRMS (those who are stable on DMT and want to discontinue therapy) regarding the need for ongoing follow-up and periodic reevaluation of the decision to discontinue DMT.
- Advise that patients who are stable (no relapses, no disability progression, stable imaging) on DMT should continue their current treatment unless the patient and physician decide a trial off therapy is warranted.
- Assess the likelihood of future relapse in individuals with SPMS by assessing patient age, disease duration, relapse history, and MRI-detected activity (eg, frequency, severity, time since most recent relapse or gadolinium-enhanced lesion).
- Review risks of continuing vs stopping DMTs in patients with CIS using DMTs who have not been diagnosed with MS.

**NOTES**
Key: AE = adverse effect; CIS = clinically isolated syndrome; EDSS = Expanded Disability Status Scale; JCV = John Cunningham virus; PML = progressive multifocal leukoencephalopathy; PPMS = primary progressive multiple sclerosis; REMS = risk evaluation and mitigation strategies; RRMS = relapsing-remitting multiple sclerosis; SPMS = secondary progressive multiple sclerosis.

**REFERENCE**