Malaysian Consensus Statement for the Treatment of Multiple Sclerosis 2025: Quick Reference Guide

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Malaysian Society of Neurosciences
Persatuan Neurosains Malaysia

Disclaimer

This quick reference guide is intended for informational purposes only and provides a summary of key points. It is not a substitute for the complete document.

For comprehensive and accurate information, please refer to the full document.

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Objective

To establish a consensus statement by experts and to provide an evidence-based updated set of recommendations for the Management of Multiple Sclerosis in Malaysia, addressing issues such as

- The choices of treatments for patients across the clinical spectrum of multiple sclerosis (MS) including clinically isolated syndrome (CIS), relapsing and progressive MS and radiologically isolated syndrome (RIS)
- Developing a standardized method for monitoring disease modifying therapy (DMT) treatment response
- Switching or discontinuation of DMTs
- Managing patients with MS (pwMS) in special situations such as MS dyscognition, pregnancy, and lactation

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Methodology

- A modified Delphi methodology was utilized to develop an evidence-based recommendations endorsed by the MOH-MOE steering committee.

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Original Research Article

Development of an Updated National Protocol for the Use of Disease-Modifying Treatments in Multiple Sclerosis: A MOH-MOE Steering Committee Initiative in Malaysia

Shridevi Subramaniam[1], Shanthi Viswanathan[2*], Suhailah Abdullah[3], Hui-Jan Tan[4], Rabani Remli[4], Norzaini Rose Mohd Zain[5], Kok-Yoon Chee[6], Sanihah Abdul Halim[7], Sin-Hong Chew[8], Shin-Yee Chey[9], Hairuddin Achmad[10], Shalini Bhaskar[11], Mohd Sufian Adenan[2], Wan Aliaa Wan Sulaiman[12], Masita Arip[13], Ai-Leen Tan[14], Farah Waheeda Tajurudin[15], Shelina Oli Mohamed[16], Su-Yin Lim[17], Rizal Aminuddin[18]

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Early initiation of Disease Modifying Therapies (DMTs)

- Patients with relapsing MS should be offered **early treatment** with DMTs as soon as **a clear diagnosis** is made.
- Patients with **highly active or aggressive disease** activity should be advised to **start treatment as soon as possible.**
- All eligible and agreeable MS patients who pass the pre-screen should be started on MS DMTs **within 2 months of diagnosis.**

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Clinically Isolated Syndrome (CIS)

- Decision to treat with DMTs should be individualized for true CIS at high risk for MS
- Patients with multiple poor prognostic factors may benefit from early initiation of high efficacy therapy (HET)

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Treatment of Acute Relapse

- The panel recommends the use of IV methylprednisolone at a daily dose of 500 – 1000mg per day for 3 – 5 days
- For patients who do not respond to initial steroid therapy, therapeutic plasma exchange (TPE) or immunoadsorption (IA) can be considered

Radiologically Isolated Syndrome (RIS)

- The decision to treat RIS requires careful deliberation of risk for further disease and needs to be individualized

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Treatment in patients with active RRMS

- DMTs, particularly HETs, should be offered without delay to patients with active RRMS based on risk stratification
- Alemtuzumab should be reserved for patients with highly active or fulminant cases of MS in view of its side effect profile

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HETs in MS

- **Relapsing MS** patients with multiple **poor prognostic factors and high disease activity should be offered HETs early**
- Patients with low or modest disease activity may be offered high efficacy treatments especially if it is their preference

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Classification of DMTs for RRMS

Classification	DMT
Moderate efficacy therapies (MET) for relapsing-remitting multiple sclerosis	Dimethyl fumarate*†
	Teriflunomide
	Interferon beta-1a (44 µg subcutaneous)
	Glatiramer acetate*
High efficacy therapies (HET) for relapsing-remitting multiple sclerosis	Alemtuzumab#
	Ofatumumab#
	Ublituximab*#
	Natalizumab*† #
	Ocrelizumab#
	Rituximab # ‡
	Cladribine
	Fingolimod
	Ozanimod*
	Ponesimod*

Classification of DMTs for PMS

Classification	PMS
Therapies for early primary progressive multiple sclerosis (PPMS)a	Ocrelizumab
	Rituximab‡
Therapies for active secondary progressive multiple sclerosis (SPMS)	Siponimod*
	Ocrelizumab
	Alemtuzumab
	Ofatumumab
	Natalizumab*†
	Rituximab‡
	Cladribine
	Teriflunomide
	Glatiramer acetate*
	Interferon beta

*Not currently registered in Malaysia †Currently available via Special Medicine Approval ‡The use of rituximab in multiple sclerosis is off-label
NB: There is a lack of evidence for efficacy of drugs in progressive MS except for ocrelizumab and siponimod

DMTs in highly active RRMS

- Patients with highly active RRMS, including those naïve to treatment, should be offered HETs

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Fulminant aggressive MS

- Patients with fulminant aggressive disease should be offered very HET such as Alemtuzumab, Natalizumab, Ofatumumab, Ocrelizumab or Rituximab* depending on availability or accessibility (see algorithm)

- If there is a lack of response to one type of HET, a shift to another HET with different mechanism of action may be tried

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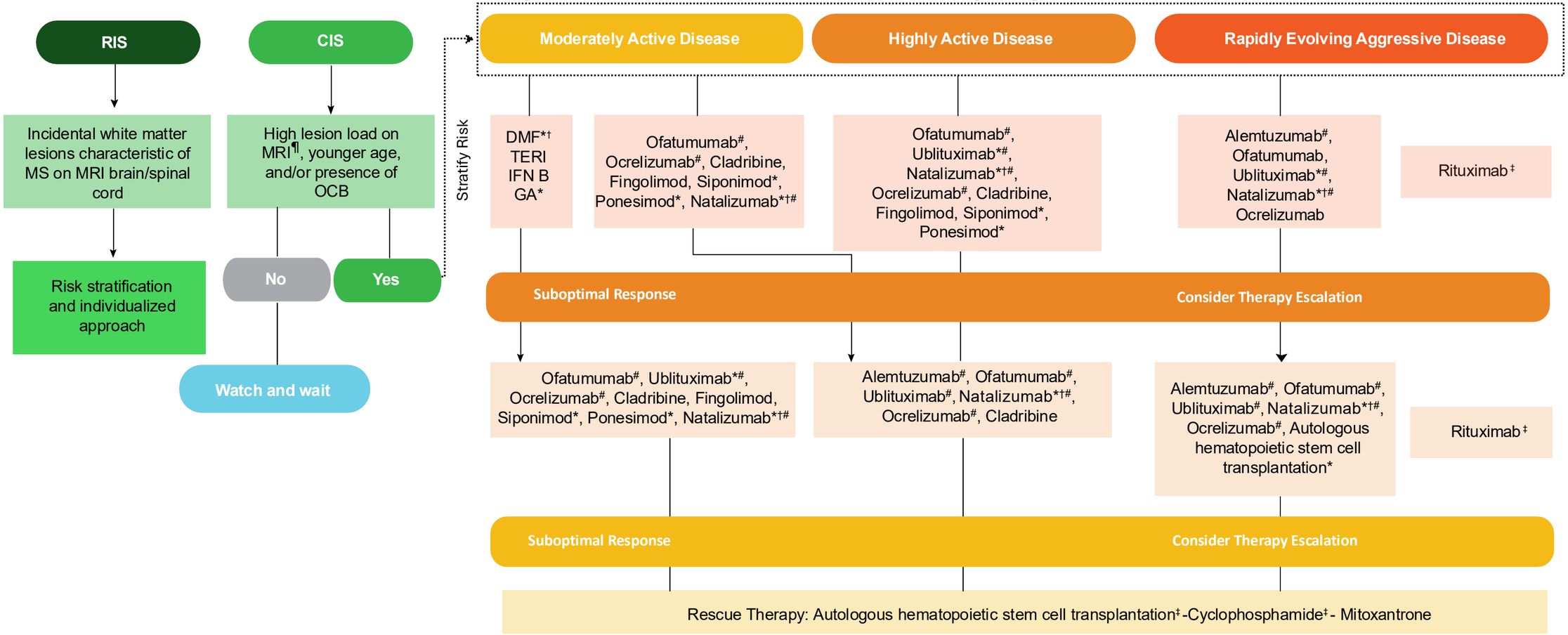
*The use of rituximab in MS is offlabel

Algorithm for Disease Modifying Treatment of CIS and RRMS



*Not currently registered in Malaysia, †Currently available via Special Medicine Approval, ‡The use of rituximab in multiple sclerosis is off-label, #These drugs are considered very high efficacy therapies , ¶ Typical lesions in the brain and spinal cord characteristic of MS
Abbreviations: CIS, clinically isolated syndrome; DMF, dimethyl fumarate; GA, glatiramer acetate; IFN B, interferon beta; OCB, oligoclonal bands; RIS, radiologically isolated syndrome; RRMS: Relapsing-remitting Multiple Sclerosis; Teri: Teriflunomide

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DMTs in Secondary Progressive MS (SPMS) and Primary Progressive MS (PPMS)

- SPMS patients, may be offered treatment with any of the MET or HET depending on whether they are newly diagnosed or progressing from relapsing MS (see table)
- Patients with PPMS may benefit from ocrelizumab and off label rituximab though the evidence is limited

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Monitoring

A combination of parameters to assess treatment response including

- Clinical relapses,
- MRI activity such as new/enlarging/+Gado enhancing lesions (in the brain and spinal cord)
- EDSS
- Timed 25 foot walk.

- Patients on stable maintenance DMTs should be seen at least every 4-6 months by a neurologist and followed up with clinical evaluation, EDSS and annual MRI

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Treatment Failure

- It is vital to allow adequate time for DMTs to produce their full benefit which may take between **6 months to 1 year**
- Patients on MET who have persistent disease activity despite treatment adherence for at least one year should have treatment escalation to HET
- Patients on existing HET who have persistent disease activity can be switched to another HET with a different MOA

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Recommendations for Switching Therapies for Treatment Failure

Initial therapy	Switching therapy
Moderate Efficacy Therapy	• Escalation to high-efficacy treatment, such as alemtuzumab, B cell depleting therapies (ofatumumab, ocrelizumab, rituximab [off-label]), fingolimod or natalizumab
High Efficacy Therapy	• Lateral shift among alemtuzumab, B-cell depleting therapies, natalizumab, cladribine and S1P modulators • If refractory or highly aggressive MS consider VHET, cyclophosphamide, mitoxantrone, or AHSCT
Alemtuzumab	• For suboptimal response after 2 years, administering a third course of alemtuzumab or switching to a different VHET is recommended
Cladribine	If treatment failure occurs: • **Within 2 years:** If not fulminant/aggressive disease, complete the full course or switch to a different HET. If fulminant or aggressive disease, switch to a VHET • **Years 3-4:** Administer 3rd cladribine course or switch to a different HET • **Year 5 and beyond:** Considered as initial cladribine responders, may repeat the full course of cladribine treatment or switch to a different HET

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Pregnancy

- Women with MS keen to conceive should have disease activity under control for at least ≥ 1year before trying to get pregnant
- If not planning a pregnancy, all women with MS should be advised on the use of contraception whilst on DMTs
- DMT use in pregnancy should be individualized balancing between manufacturer's recommendations, guidelines/post marketing and real-world data

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Breastfeeding

- Only interferons and GA are safe during breastfeeding.
- Ocrelizumab, ofatumumab and rituximab may be used with caution and monitoring of infant during breastfeeding

DMT Use In Pregnancy and Breastfeeding

DMT	Discontinuation before pregnancy	When to stop DMT before pregnancy	Pregnancy	Breastfeeding
GA	Continue		Compatible	Compatible
IFN-B	Continue		Compatible	Compatible
Dimethyl Fumarate	May continue until pregnancy is confirmed		Caution	Caution
Teriflunomide	Discontinue	Charcoal / cholestyramine washout For 11 days till the level < 0.02mg/L	Contraindicated	Contraindicated
Fingolimod	Discontinue	2 months	Contraindicated	Contraindicated
Cladribine	Discont inue	6 months	Contraindicated	Contraindicated During and 1 week after last dose
Alemtuzumab	Discontinue	4 months	Contraindicated	Caution* Start 4 months after last infusion
Natalizumab†	May continue, especially in Highly Active cases		Continue with extended dosing interval of 6-8 weeks till 30-34 weeks of gestation	Caution* Very low concentration in breastmilk
Rituximab#	Discont inue	Once pregnancy is confirmed or 3 months before conception	Caution	Caution*
Ofatumumab	Discont inue	Once pregnancy is confirmed	Caution*	Caution* Very low concentration in breastmilk
Ocrelizumab	Discont inue	Once pregnancy is confirmed or 3 months before conception	Caution*	Caution* Very low concentration in breastmilk

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Cognition

- Early DMT initiation may have an effect on preservation or delaying cognitive deterioration
- Neurologists should screen pwMS for cognitive deterioration with standard tools such as the Symbol Digit Modality Test (SDMT) where available and other validated assessment tools for cognitive testing
- PwMS who exhibit cognitive impairment should be managed through a multidisciplinary approach, including a neurologist, and where appropriate, a neuropsychiatrist or psychiatrist, and a clinical psychologist or neuropsychologist

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Treatment Discontinuation

- PwMS who have stable disease on a given DMT may continue therapy including HET regardless of age
- The decision to continue, de-escalate or discontinue treatment needs to be carefully assessed on an individual basis
- In active disease, discontinuing or pausing treatment at a **patient's explicit request** may be done if adhering to clear guidelines for clinical and imaging monitoring, and counselling about the risk of rebound especially with fingolimod and natalizumab
- If the patient continues to progress over time and becomes severely disabled, and develops life-limiting co-morbidities, treatment discontinuation **may** be considered following counselling

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Health and Wellbeing

- It is important to emphasize healthy living, smoking avoidance, identification and management of comorbidities, and maintain mental wellbeing as well as provision of exercise in pwMS

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Vitamin D Supplementation

- PwMS should have baseline levels of vitamin D done to determine deficiency
- PwMS may be supplemented with oral vitamin D to maintain levels at 75 – 125 nmol/L
- For those who are vitamin D deficient (levels < 50 nmol/L), replacement dose should be given (e.g. 50,000 IU of vitamin D3 per week for 8 to 12 weeks)

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Abbreviations

CIS, clinically isolated syndrome

DMT, disease modifying therapy

EDSS, expanded disability status scale

GA, glatrimer acetate

HET, high efficacy therapy

IA, immunoadsorption

MET, moderate efficacy therapy

MOA, mechanism of action

MRI, magnetic resonance imaging;

MS, multiple sclerosis

pwMS, patient with MS

RIS; radiologically isolated syndrome

RRMS, relapse remitting MS

SDMT, symbol digit modality test

SPMS, secondary progressive MS

TPE, therapeutic plasma exchange

VHET, very high efficacy therapy

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A collaborative effort by the Ministry of Health, Ministry of Education, Private Hospitals and MS Society of Malaysia

We would like to thank all the contributors and reviewers for making this consensus statement document possible

Available on the MSN website:

www.neuro.org.my

Support for the development of this quick reference guide companion document to the full consensus statement has been provided by:

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