Appendix 10_Results of the consensus process

START ROUND 1 (e-mail): A total of 18 statements were circulated:
- 2 statements were accepted without further modification
- 16 were modified based on comments made by the experts
- 2 new statement was proposed

END ROUND 1:
- 2 statements were incorporated in the GL document
- 18 statements were considered for consensus in round 2

START ROUND 2 (face to face meeting): A total of 18 statements (16 modified + 2 new) were considered for consensus:
- 9 were accepted without further modification
- 6 were accepted after small modifications
- 3 were postponed to a 3rd round of consensus because of time limitations

END ROUND 2:
- 15 statements were incorporated in the GL document
- 3 statements were considered for round 3

START ROUND 3 (e-mail): Three statements were circulated:
- 2 statements were accepted without further modification
- 1 statement was accepted after small modifications

END ROUND 3:
- 3 statements were incorporated in the GL document

	Final agreement*			
Statement	Low (1-3)	Medium (4-6)	High (7-9)	
R1. The entire spectrum of DMDs should be prescribed only in centres with adequate infrastructure to provide: - Proper monitoring of patients - Comprehensive assessment - Detection of side effects and ability to promptly address them.			100%	Consensus statement
R2. Offer interferon or glatiramer acetate to patients with CIS and an abnormal MRI with lesions suggestive of MS who do not fulfil MS criteria.		18.2%	81.8%	Strong recommendation
R3. Offer early treatment with DMDs in patients with active relapsing-remitting MS as defined by clinical relapses and/or MRI activity (active lesions -contrast-enhancing lesions; new or unequivocally enlarging T2 lesions assessed at least annually). Also includes CIS fulfilling current diagnostic criteria of MS.		5.9%	94.1%	Strong recommendation
R4. For active relapsing-remitting MS, choosing between the wide range of available drugs (interferon beta-1b, interferon beta-1a -sc, im-, peginterferon beta-1a, glatiramer acetate, teriflunomide, dimethyl fumarate, cladribine, fingolimod, daclizumab, natalizumab, alemtuzumab and ocrelizumab), from the modestly effective to the highly efficacious, will depend on the following factors, in discussion with the patient: - Patient characteristics and comorbidities - Disease severity/activity - Drug safety profile - Accessibility of the drug		5.9%	94.1%	Consensus statement
R5. Consider treatment with interferon-1a (sc) or -1b in patients with active SPMS taking into account, in discussion with the patient, the efficacy, safety, and tolerability profile of these drugs.		18.2%	81.8%	Weak recommendation
R6. Consider treatment with mitoxantrone in patients with active secondary progressive MS taking into account, in discussion with the patient, the efficacy, and specifically the safety and tolerability profile of this agent.		18.2%	81.8%	Weak recommendation
R7. Consider treatment with ocrelizumab or cladribine for patients with			100%	Weak recommendation

active secondary-progressive MS.				
R8. Consider treatment with ocrelizumab for patients with primary-progressive MS.			100%	Weak recommendation
R9. Consult the Summary of Product Characteristics (SPC) for dosage, special warnings and precautions for use, contraindications, and monitoring of side effects and potential harms.			100%	Consensus statement
R10. Consider combining MRI with clinical measures when evaluating disease evolution in treated patients.			100%	Consensus statement
R11. When monitoring treatment response in patients treated with DMDs, perform a standardized reference brain MRI usually within six 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, taking into account the following aspects: - the drug's mechanism of action (particularly the speed of action) - disease activity (including clinical and MRI measures)		17.6%	82.4%	Consensus statement
R12. 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 gadolinium enhancing lesions for monitoring treatment response. Evaluation of these parameters requires: - high-quality, standardized MRI scans - interpretation by highly qualified readers with experience in MS			100%	Consensus statement
R13. When monitoring treatment safety in patients treated with DMDs, perform a standardized reference brain MRI: - every year in low risk PML patients - more frequent MRIs (on a 3 to 6 monthly basis) in high risk PML patients (JCV positive, natalizumab treatment duration over 18 months) - 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.			100%	Consensus statement
R14. Offer a more efficacious drug to patients treated with interferon or glatiramer acetate who show evidence of disease activity assessed as recommended in questions 4-5 of this guideline.			100%	Strong recommendation

R15. When deciding on which drug to switch to, in consultation with the patient, consider the following factors: - Patient characteristics and comorbidities - Drug safety profile - Disease severity/activity			100%	Consensus statement
R16. When treatment with a highly efficacious drug is stopped, either due to inefficacy or safety concerns, consider starting another highly efficacious drug. When starting the new drug, take into account the following factors: - Disease activity (clinical and MRI), the greater the activity, the higher the urgency to start new treatment. - Half life and biological activity of the previous drug. - The potential for resumed disease activity or even rebound (particularly with natalizumab).			100%	Weak recommendation
R17. In treatment decisions, clinicians should consider the possibility of resumed disease activity or even rebound when stopping treatment, particularly with natalizumab.			100%	Strong recommendation
R18. Consider continuing a DMD if a patient is stable (clinically and on MRI) and shows no safety or tolerability issues.		10%	90%	Weak recommendation
R19. Advise all women of childbearing potential that DMDs are not licensed for pregnancy, except glatiramer acetate 20 mg/ml.			100%	Consensus statement
R20. For women planning a pregnancy, if there is a high risk of disease reactivation, consider using interferon or glatiramer acetate until pregnancy is confirmed. In some very specific (active) cases, continuing this treatment during pregnancy could also be considered.			100%	Weak recommendation
R21. For women with persistent high disease activity, it would generally be advised to delay pregnancy. For those who, despite this advice, still decide to become pregnant or have an unplanned pregnancy: -Treatment with natalizumab throughout pregnancy may be considered after full discussion of potential implications. -Treatment with alemtuzumab could be an alternative therapeutic option for		12%	88%	Weak recommendation

planned pregnancy in very active cases, provided that a 4-month interval is strictly observed from the latest infusion until conception.				

*Based on the result of the Likert scale grouped into 3 categories (1–3: inappropriate strategy; 4–6: uncertain; 7–9: appropriate strategy). Agreement cut-off point 80%