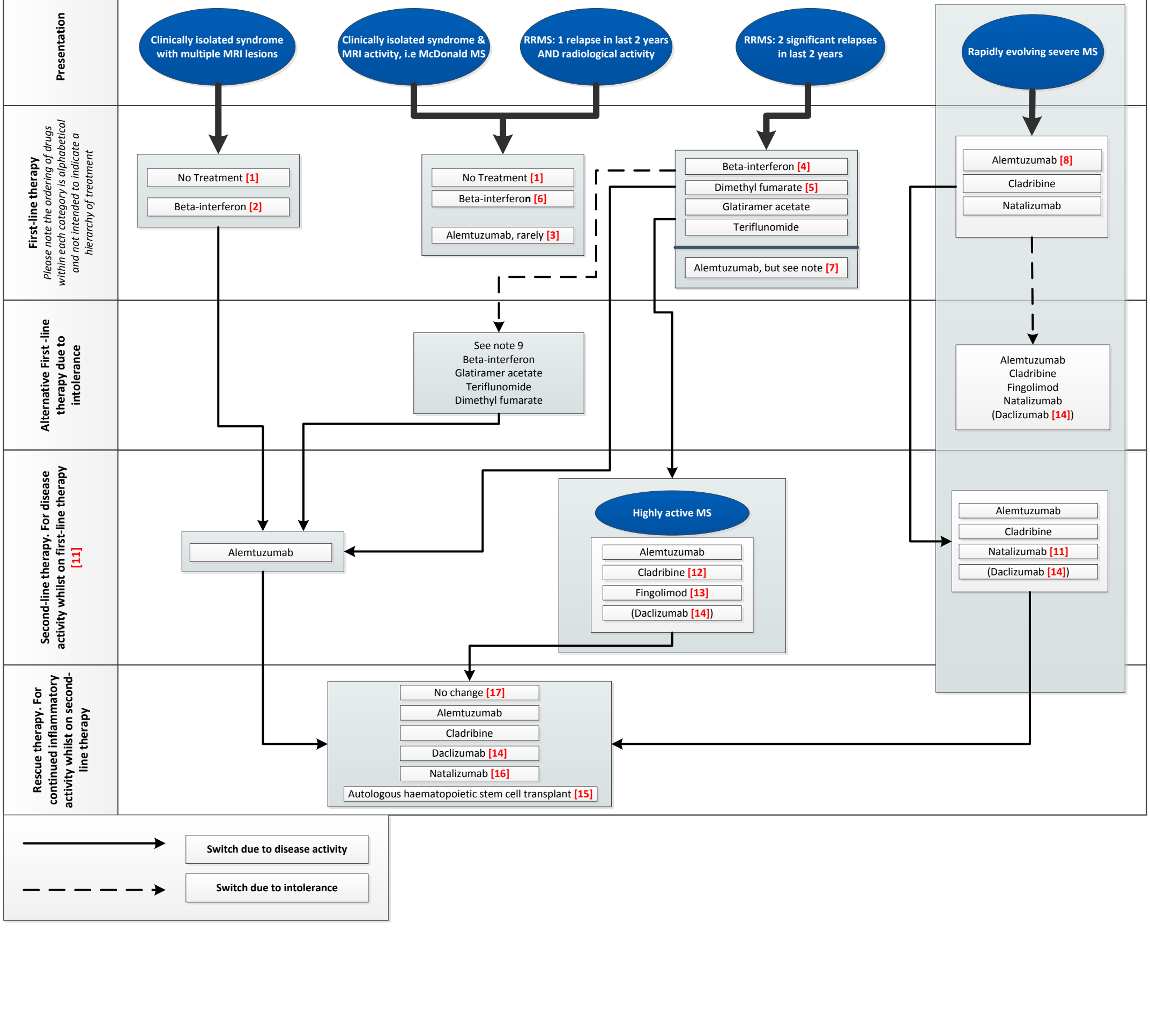
Treatment Algorithm for Multiple Sclerosis Disease-modifying Therapies

(Please note the ordering of drugs within each category is alphabetical and not intended to indicate a hierarchy of treatment)



Notes

1. Trials of first-line therapies in people with CIS at high risk of conversion have NOT shown a convincing long-term effect on the accumulation of disability. Therefore it is reasonable to opt for no treatment in many patients in this situation.
2. Under 2014 NHS England guidance, beta-interferon may be offered for patients within 12 months of a clinically significant clinically isolated syndrome when MRI evidence predicts a high likelihood of recurrent episodes (i.e. development of MS).
3. In exceptional circumstances, clinical or radiological markers may indicate a poor prognosis for rapidly developing permanent disability even after just one clinical episode, in which case, alemtuzumab may be considered. Physicians and patients should weigh up the considerable risks and burden of monitoring associated with this drug, against the potential benefit
4. For RRMS (that is not RES), beta-interferon, glatiramer and teriflunomide are effective and safe.
5. There is some evidence that dimethyl fumarate may be more effective at suppressing relapses than beta-interferon, glatiramer and teriflunomide
6. NHS England 2014 policy allowed the use of beta-interferon in "patients with only a single major relapse in the preceding two years, but combined with MRI evidence of continuing disease activity"
7. For RRMS (that is not RES), alemtuzumab is an option that may be considered, but we note it is considerably more high-risk than the other options. It should be used only when the patient and MS specialists accept the significant risks and burden of monitoring.
8. Alemtuzumab and cladribine may be considered – by some patients and clinicians – a safer option that natalizumab when JC virus serology is high-index positive.
9. If a patient satisfies the eligibility criteria for a first-line therapy, and then is relapse-free on a drug to which he/she becomes intolerant, they may be switched to another DMT even though their relapses may now fall outside the eligibility window.
10. NHS England 2014 policy states that fingolimod can be used an alternative to natalizumab for those patients receiving natalizumab who are at high risk of developing progressive multifocal leukoencephalopathy (PML) as defined by: (i) JCV exposure indicated by anti-JCV antibody positive status, (ii) Receiving an immunosuppressant prior to receiving natalizumab, or (iii) Natalizumab treatment duration of >2 years. If patients develop a severe adverse effect to natalizumab (e.g. anaphylaxis), and they have not previously received fingolimod, then it may be appropriate to use fingolimod.
11. Definition of disease activity: treatment failure may be indicated by either clinical or radiological relapse-related changes, after significant exposure to the treating drug, with changes indicating a poor prognosis for future disability. For instance, alemtuzumab is specifically licensed for "active disease defined by clinical or imaging features."
12. For cladribine, NICE specifically defined treatment failure as "1 relapse in the previous year and MRI evidence of disease activity."
13. For fingolimod: under previous guidance, fingolimod may be given if patients have an unchanged or increased relapse rate or ongoing severe relapses compared with the previous year despite treatment with beta interferon or glatiramer acetate. This is now extended to include disease activity on teriflunomide and dimethyl fumarate.
14. In October 2017, the EMA restricted use of daclizumab to "adult patients with highly active relapsing disease despite a full and adequate course of treatment with at least two disease modifying therapies and cannot be treated with other DMTs or with rapidly evolving severe relapsing multiple sclerosis who are unsuitable for treatment with other DMTs."
15. Autologous haematopoietic stem treatment for autoimmunity is commissioned at specialised centres and is currently being offered to some people with MS in some parts of the UK. But there is not yet adequate controlled trial of its efficacy relative to other potent therapies. We recommend that it is made available equitably to all people with MS, but we propose that it should only be considered for people with relapsing disease (not progressive) who have failed high-activity licensed disease modifying therapies, and are prepared to accept the significant risks of the procedure. We recommend that this treatment is offered only by units with expertise both in the management of aggressive multiple sclerosis and the use of autologous haematopoietic stem treatment.
16. The risk of PML on natalizumab is likely to be increased after alemtuzumab or cladribine, given the prolonged lymphopenia induced by these drugs. But, where the patient is negative for JC serology, this may be appropriate.
17. After considering all these options, it may be appropriate to continue the second-line therapy, despite evidence of disease activity.