Summary of Disease-Modifying Therapies (DMT) options in Multiple Sclerosis

Grouping is alphabetical and not intended to indicate hierarchy or order of use. Consider patient choice and patient specific factors, including family planning, in treatment decisions.

Single clinical episode with radiological activity [see note 7.1]

Single clinical episode *not* fulfilling McDonald criteria for RRMS

- No treatment

Single clinical episode fulfilling McDonald criteria for RRMS

- No treatment
- Cladribine [7.2]*
- Glatiramer acetate
- Interferon beta 1a
- Ocrelizumab [7.1]*
- Ofatumumab [7.1]*
- Ponesimod
- Ublituximab [7.1]*

Primary Progressive Multiple Sclerosis (PPMS)

PPMS

- Ocrelizumab

Secondary Progressive Multiple Sclerosis (SPMS)

Active secondary progressive disease

- Interferon beta 1b++
- Siponimod

Relapsing – Remitting Multiple Sclerosis (RRMS)

RRMS 1 relapse in last 2 years AND radiological activity

- Cladribine*
- Glatiramer acetate
- Interferon beta 1a
- Ocrelizumab*
- Ofatumumab*
- Ponesimod
- Ublituximab*

RRMS 2 relapses in last 2 years

- Cladribine*
- Dimethyl fumarate
- Diroximel fumarate
- Glatiramer acetate
- Interferon beta 1a
- Interferon beta 1b++
- Ocrelizumab *
- Ofatumumab *
- Ponesimod
- Teriflunomide
- Ublituximab*

Rapidly evolving severe (RES) RRMS*

- Alemtuzumab [8.2]*
- Cladribine [8.1, 8.2 & 9.2]*
- Natalizumab*
- Ocrelizumab [8.2]*
- Ofatumumab [8.2]*
- Ublituximab [8.2]*

Alternative first line

- Fingolimod [9.3]*

Notes – see full policy for details

Treatments with [*] suffix should be agreed at MDT as should all treatments in children or complex cases (see policy section 2).

Intolerance to treatment; [Note 9.1] If a patient satisfies the eligibility criteria for a first line therapy, and then is relapse-free on a drug to which they become intolerant then they may be switched to another DMT within group even though their relapses may now fall outside the eligibility window.

[Note 7.1] Where clinical or radiological markers indicate a poor prognosis for rapidly developing permanent disability, **cladribine**, **ofatumumab, ocrelizumab** or **ublituximab** may be considered after a single clinical episode with MRI activity. Physicians and patients should weigh up the risks against the potential benefit. This must be agreed by the MDT.

[Note 7.2] & [Notes 8.1, 9.2, 10.1 & 11.1] **Cladribine** is allowed following NICE TA1053 for people who have active relapsing-remitting multiple sclerosis, and when high-efficacy disease-modifying therapies would be offered

[Note 8.2] **Alemtuzumab**, **cladribine**, **ocrelizumab**, **ofatumumab** or **ublituximab** may be a safer option than **natalizumab** where John-Cunnigham Virus (JCV) serology is high-index positive

[Note 9.3] **Fingolimod** can be used as alternative to **natalizumab** for patients receiving **natalizumab** who are at high risk of developing Progressive Multifocal Leukoencephalopathy (PML), as defined by the following;

(i) JCV exposure indicated by anti-JCV antibody positive status,

(ii) Receiving an immunosuppressant prior to receiving **natalizumab**, or

(iii) **Natalizumab** treatment duration > 2 year

If patient develops a severe adverse effect to natalizumab (e.g. anaphylaxis), and they have not previously received **fingolimod**, then it may be appropriate to use **fingolimod**.

[Note 10.2] For **fingolimod**, under previous guidance, **fingolimod** may be given if patients have an unchanged or increased relapse rate, or ongoing severe relapses compared to the previous year despite treatment with **beta interferon** or **glatiramer acetate**. This is now extended to include disease activity on **dimethyl fumarate**, **diroximel fumarate**, **teriflunomide** and **ponesimod**.

[Note 10.3] & [Note 11.2] Autologous haematopoietic stem cell treatment for autoimmunity is commissioned at specialised centres and should be discussed at a specialist MDT. See policy for links. A minimum requirement is significant disabling clinical relapse with new MRI activity in the last 12 months on higher efficacy DMT (**alemtuzumab**, **natalizumab**, **ocrelizumab**, **ofatumumab** , **ublituximab** and in some cases **cladribine**).

[Note 10.4] & [Note 11.4] Following NICE TA1126 **natalizumab** (subcutaneous originator or intravenous biosimilar) can be used in highly active relapsing–remitting multiple sclerosis in adults if it has not responded to a full and adequate course of at least 1 disease-modifying therapy and the characteristics of the person and the activity of their MS mean that **cladribine** is not suitable

[Note 11.3] After considering all options, it may be appropriate to continue the second line therapy, despite evidence of disease activity. None of the treatments promise 100% efficacy and some patients and clinicians may choose to tolerate some disease activity without changing treatments.

++ **Interferon beta 1b** ; Currently only available as ***Betaferon***®. ***Betaferon***® is not approved by NICE for active secondary progressive multiple sclerosis (NICE TA527) but can be used under clinical discretion for secondary progressive multiple sclerosis.

Disease activity on treatment or progression to Rapidly Evolving Severe (RES)-RRMS

Disease activity whilst on 1st line DMT for RRMS

- AHSCT [10.3]*
- Alemtuzumab*
- Cladribine [10.1]*
- Fingolimod [10.2]*
- Natalizumab [10.4]
- Ocrelizumab*
- Ofatumumab*
- Ponesimod*
- Ublituximab*

Disease activity whilst on 1st line DMT for RES-RRMS *or* develops RES-RRMS whilst on 1st line DMT for RRMS

- AHSCT [10.3]*
- Alemtuzumab*
- Cladribine [10.1]*
- Natalizumab [10.4]*
- Ocrelizumab*
- Ofatumumab*
- Ublituximab*

Disease activity on treatment or progression to Rapidly Evolving Severe (RES)-RRMS

Disease activity whilst on 2nd line DMT for RRMS

- No change [11.3]*
- AHSCT [11.2]*
- Alemtuzumab*
- Cladribine [11.1]*
- Natalizumab [11.4]
- Ocrelizumab*
- Ofatumumab*
- Ublituximab*

Disease activity whilst on 2nd line DMT for RES-RRMS *or* develops RES-RRMS whilst on 2nd line DMT for RRMS

- No change [11.3]*
- AHSCT [11.2]*
- Alemtuzumab*
- Cladribine [11.1]*
- Natalizumab [11.4]*
- Ocrelizumab*
- Ofatumumab*
- Ublituximab*