Multiple sclerosis - (MS) [relapsing remitting multiple sclerosis (RRMS)]

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Condition for which IVIg use is in exceptional circumstances only

Specific Conditions	• Relapsing remitting multiple sclerosis
Indication for IVIg Use	• Severe relapse of clinically definite relapsing remitting multiple sclerosis (RRMS) with no response to high dose methylprednisolone or where methylprednisolone is contraindicated • Prevention of relapse of clinically definite relapsing remitting multiple sclerosis (RRMS) where alternative therapies are inappropriate, unavailable or contraindicated
Level of Evidence	Evidence of probable benefit – more research needed (Category 2a)
Description and Diagnostic Criteria	Multiple sclerosis (MS) is a chronic disorder of the central nervous system (CNS) characterised by a triad of inflammation, demyelination and gliosis. Lesions of MS, known as plaques, are typically disseminated in time and location throughout the brain and spinal cord. Four clinical types of MS have been described: relapsing/remitting MS (RRMS), primary progressive MS (PPMS), secondary progressive MS (SPMS), and progressive/relapsing MS (PRMS). New evidence and consensus in 2010 has led to further revision of the McDonald Criteria for diagnosis of multiple sclerosis. The use of imaging for demonstration of dissemination of central nervous system lesions in space and time is defined. The 2010 revisions simplify the diagnostic criteria, maintain their diagnostic sensitivity and specificity and support earlier diagnosis and more uniform and widespread use (Polman et al 2011).
Justification for Evidence Category	While literature and systematic reviews in 2004 and 2006 demonstrate probable benefit, there are a broad range of licenced therapeutics now available to treat multiple sclerosis (MS) and in particular, relapsing/remitting MS (RRMS), with evidence supported by large randomised controlled trials. Such evidence indicates that intravenous immunoglobulin (IVIg) use in MS should be limited to exceptional circumstances only and there is no longer a role for IVIg in the continuing treatment of MS. IVIg may be indicated in treatment of relapses where there are severe disabling consequences of the attack (e.g. paraparesis or blindness). For more information see: Therapeutic approaches to disease modifying therapy for multiple sclerosis in adults: an Australian and New Zealand perspective: part 3 treatment practicalities and recommendations Journal of Clinical Neuroscience 2014.
Diagnosis Requirements	A diagnosis must be made by a Neurologist.
Qualifying Criteria for IVIg Therapy	Severe relapse of clinically definite relapsing remitting multiple sclerosis (RRMS) with no response to high dose methylprednisolone or where methylprednisolone is contraindicated • Severe relapse of clinically definite relapsing remitting MS (RRMS) proven by brain or spinal cord magnetic resonance imaging (MRI) scan and at least two relapses in the previous two years AND • Unresponsive to a course of high dose methylprednisolone treatment OR • Methylprednisolone treatment is contraindicated **Note:** There are numerous immunomodulatory therapies available for multiple sclerosis. IVIg is not available for routine ongoing treatment for patients with MS.

Prevention of relapse of clinically definite relapsing remitting multiple sclerosis (RRMS) where alternative therapies are inappropriate, unavailable or contraindicated

- Clinically definite relapsing remitting multiple sclerosis (RRMS) proven by brain or spinal cord MRI scan and at least two relapses in the previous two years

  AND

- The patient remains ambulant as measured by an Expanded Disability Status Scale (EDSS) score to a maximum value of 6.5 points

  AND

- Disease activity is resistant to all other therapies listed below or therapies are unavailable or are contraindicated
  - Methylprednisolone
  - Plasmapheresis exchange
  - Fingolimod (Gilenya)
  - Copoxone (glatiramer acetate)
  - Interferon beta (Avonex, Betaferon, Rebif)
  - Dimethyl fumerate (Tecfidera)
  - Natalizumab (Tysabri)
  - Teriflunomide (Aubagio)
  - Alemtuzumab (Lemtrada)

Review by a neurologist is required every six months. Documentation of clinical effectiveness is necessary for continuation of IVIg therapy.

Effectiveness can be demonstrated by objective findings of improvement in relapse rate in comparison to pre-treatment levels.

After a maximum of 12 months treatment, patients should be re-assessed as to whether a more appropriate treatment is avaialble. A new authorisation request will be required for any subsequent course (after 12 months) as appropriate.

Exclusion Criteria

Primary progressive MS
Progressive phase of MS without relapses

Review Criteria for Assessing the Effectiveness of IVIg Use

Severe relapse of clinically definite relapsing remitting multiple sclerosis (RRMS) with no response to high dose methylprednisolone or where methylprednisolone is contraindicated

Review is not mandated for this indication however the following criteria may be useful in assessing the effectiveness of Ig therapy

- Evidence of improvement in relapse rate in comparison to pre-treatment levels

Note: There are numerous immunomodulatory therapies available for multiple sclerosis. IVIg is not available for routine ongoing treatment for patients with MS.

Prevention of relapse of clinically definite relapsing remitting multiple sclerosis (RRMS) where alternative therapies are inappropriate, unavailable or contraindicated

Review by a neurologist is required every six months. Documentation of clinical effectiveness is necessary for continuation of IVIg therapy.

Effectiveness can be demonstrated by objective findings of improvement in relapse rate in comparison to pre-treatment levels.

After a maximum of 12 months treatment, patients should be re-assessed as to whether a more appropriate treatment is available. A new authorisation request will be required for any subsequent course (after 12 months) as appropriate.

Clinical effectiveness of Ig therapy may be demonstrated by:

- No evidence of relapsing remitting MS (RRMS) disease progression while on Ig treatment as measured by an Expanded Disability Status Scale (EDSS) score to a value equal to or less than the qualifying score

  AND

- Other therapies remain ineffective or unavailable and a valid reason to continue Ig treatment is provided

Note: There are numerous immunomodulatory therapies available for multiple sclerosis. IVIg is not available for routine ongoing treatment for patients with MS.

Dose	
	Severe relapse of clinically definite relapsing remitting multiple sclerosis (RRMS) with no response to high dose methylprednisolone or where methylprednisolone is contraindicated • **Induction Dose** - 1–2 g/kg in 2 to 5 divided doses The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient. Refer to the current product information sheet for further information on dose administration and contraindication. **Note:** There are numerous immunomodulatory therapies available for multiple sclerosis. IVIg is not available for routine ongoing treatment for patients with MS.
	Prevention of relapse of clinically definite relapsing remitting multiple sclerosis (RRMS) where alternative therapies are inappropriate, unavailable or contraindicated • **Induction Dose** - 1–2 g/kg in 2 to 5 divided doses. • **Maintenance Dose** - 0.4–1 g/kg, 4–6 weekly. After a maximum of 12 months treatment, patients should be re-assessed as to whether a more appropriate treatment is available. A new authorisation request will be required for any subsequent course (after 12 months) as appropriate. The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient. Refer to the current product information sheet for further information on dose, administration and contraindications. **Note:** There are numerous immunomodulatory therapies available for multiple sclerosis. IVIg is not available for routine ongoing treatment for patients with MS. Patients should be re-assessed as to whether more appropriate treatment is available.

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