Multiple sclerosis (MS)

Version: 2.1
Published: 06 July 2016

Condition for which IVIg has an emerging therapeutic role.

Specific Conditions	• Multiple sclerosis in pregnancy and the immediate post-partum period • Multiple sclerosis in young patients severe/relapsing/remitting in whom other therapies have failed • Multiple sclerosis - severe relapse with no response to high dose methylprednisolone
Indication for IVIg Use	• Clinically definite relapsing remitting MS during pregnancy and the immediate post-partum period when other immunomodulation is contraindicated. • Young patients with clinically definite severe relapsing remitting disease in whom other therapies have failed. • Severe relapse of clinically definite relapsing remitting MS, with no response to high-dose methylprednisolone.
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). Diagnosis requires two or more episodes of symptoms and two or more signs that reflect pathology in anatomically non-contiguous white matter tracts of the CNS. Symptoms must last >24 hours and occur as separate episodes at least one month apart. At least one of the two signs must be present on neurological examination, while the other may be detected by paraclinical tests such as intrathecal immunoglobulin G (IgG) (oligoclonal bands and visual evoked potentials).
Justification for Evidence Category	The Biotext (2004) literature review included one systematic review, six randomised controlled trials (RCTs), three case-control studies and one case-series, with a total sample size of 849. The quality of the included studies varied widely. The systematic review found some benefit from intravenous immunoglobulin (IVIg) treatment. No benefit was found in two of the RCTs (IVIg did not appear to reverse established muscle weakness), and significant benefit was reported in two RCTs. The other two RCTs were identified by Biotext from the Cochrane register of trials, but no further information about the studies was obtained. The review by Frommer and Madronio (2006) included eight high-quality RCTs and one medium-quality double-blinded controlled trial, with a total of 708 patients. These studies suggested that the occurrence of relapse may be reduced by IVIg at three years, but conclusive evidence in relation to the use of IVIg in reducing relapse rates and severity of relapse in established disease could not be demonstrated. IVIg treatment for the first year from onset of the first neurological event significantly lowered the incidence of second attacks and reduced disease activity as measured by magnetic resonance imaging (MRI). IVIg administered in monthly pulses for up to two years appeared to reduce annual exacerbation rates in patients with RRMS and SPMS, but its effect on long-

	term disability was unclear.
Diagnosis Requirements	A diagnosis must be made by a Neurologist.
Qualifying Criteria for IVIg Therapy	Clinically definite relapsing remitting MS during pregnancy and the immediate post-partum period when other immunomodulation is contraindicated. • Severe relapse with significant disability, as measured by the Expanded Disability Status Scale, MS functional scores or other functional/disability scales. Application for IVIg use for this indication maybe considered on a case-by-case basis. **Note:** There are numerous immunomodulatory therapies available for MS. IVIg is not available for routine ongoing treatment for patients with MS. Young patients with clinically definite severe relapsing remitting disease in whom other therapies have failed. • Severe relapse with significant disability, as measured by the Expanded Disability Status Scale, MS functional scores or other functional scales. AND • Other therapies have failed. Application for IVIg use for this indication maybe considered on a case-by-case basis **Note:** There are numerous immunomodulatory therapies available for MS. IVIg is not available for routine ongoing treatment for patients with MS. Severe relapse of clinically definite relapsing remitting MS, with no response to high-dose methylprednisolone. • Severe relapse with significant disability, as measured by the Expanded Disability Status Scale, MS functional scores or other functional scales. AND • No response to a course of high-dose methylprednisolone treatment. Application for IVIg use for this indication maybe considered on a case-by-case basis **Note:** There are numerous immunomodulatory therapies available for MS. IVIg is not available for routine ongoing treatment for patients with MS.
Exclusion Criteria	Primary progressive MS. Progressive phase of MS without relapses.

Review Criteria for Assessing the Effectiveness of IVIg Use

Clinically definite relapsing remitting MS during pregnancy and the immediate post-partum period when other immunomodulation is contraindicated.

Six-monthly review by a Neurologist is required.

Documentation of clinical effectiveness is necessary for continuation of Ig therapy.

On review of an authorisation request

Clinical effectiveness of Ig therapy may be demonstrated by:

- Improvement in the relapse rate and no progression of RRMS disease during the authorisation period, as measured by the Expanded Disability Status Scale, MS functional scores or other functional scales, when compared to the qualifying assessment.

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

Young patients with clinically definite severe relapsing remitting disease in whom other therapies have failed.

Six-monthly review by a Neurologist is required.

Documentation of clincial effectiveness is required for continuation of Ig therapy.

On review of an authorisation period

Clinical effectiveness of Ig therapy may be demonstrated by:

- Improvement in the relapse rate and no progression of RRMS disease, as measured by the Expanded Disability Status Scale, MS functional scores or other functional measures compared to the qualifying assessment.

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

Severe relapse of clinically definite relapsing remitting MS, with no response to high-dose methylprednisolone.

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

Clinical effectiveness of Ig therapy may be demonstrated by:

- Improvement in the relapse rate and no progression of RRMS disease, as measured by the Expanded Disability Status Scale, MS functional scores or other functional measures compared to the qualifying assessment.

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

Dose	
	Clinically definite relapsing remitting MS during pregnancy and the immediate post-partum period when other immunomodulation is contraindicated. • **Induction Dose** - 1–2 g/kg in 2 to 5 divided doses. • **Maintenance Dose** - 0.4–1 g/kg, 4–6 weekly. Aim for minimum dose to maintain optimal functional status **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.**
	Young patients with clinically definite severe relapsing remitting disease in whom other therapies have failed. • **Induction Dose** - 1–2 g/kg in 2 to 5 divided doses. • **Maintenance Dose** - 0.4–1 g/kg, 4–6 weekly. Aim for minimum dose to maintain optimal functional status **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.**
	Severe relapse of clinically definite relapsing remitting MS, with no response to high-dose methylprednisolone. • **Induction Dose** - 1–2 g/kg in 2 to 5 divided doses. Aim for minimum dose to maintain optimal functional status **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.**

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Generated on: 4 April 2019