Inflammatory myopathies: polymyositis (PM), dermatomyositis (DM) and necrotising autoimmune myopathy (NAM)

Condition for which Ig has an established therapeutic role.

Specific Conditions	• Polymyositis (PM) • Dermatomyositis (DM) • Necrotising autoimmune myopathy (NAM)
Indication for Ig Use	• Treatment of significant muscle weakness or dysphagia unresponsive to corticosteroids and other immunosuppressant agents in adults with biopsy-proven PM or DM or NAM or children with clinical, biochemical and imaging abnormalities consistent with definite PM or DM or NAM
Level of Evidence	Insufficient data (Category 4a)
Description and Diagnostic Criteria	Dermatomyositis (DM) and polymyositis (PM) are idiopathic inflammatory myopathies. Necrotizing autoimmune myopathy (NAM) typically has necrotic myofibres with less inflammatory infiltrate and the absence of direct myocyte invasion by lymphocytes. These disorders are acquired and have in common the occurrence of significant muscle weakness and the presence of an inflammatory response within the muscle. The weakness usually develops subacutely but may be chronic and present over many months. Proximal muscles are predominantly affected in a symmetric fashion. In adults, the diagnosis of DM, PM and NAM relies on the combination of careful clinical evaluation, an elevated creatine kinase level, electromyography and muscle biopsy. In children, the combination of a characteristic rash, raised muscle enzymes, an objective measure of muscle weakness e.g. Childhood Myositis Assessment Scale (CMAS) and typical MRI scan abnormalities are considered sufficient for diagnosis, with muscle biopsy reserved for atypical cases. NAM is often associated with a history of statin exposure, and the presence of autoantibodies against HMG coenzyme reductase, or other muscle antigens.
Justification for Evidence Category	**Polymyositis (PM):** The Biotext (2004) review identified one prospective case-series study of 35 adults with chronic refractory PM. This study reported clinical improvement in 71 percent of patients with significant improvement in muscle power, muscle disability scores and creatine kinase (CK) levels (p less than 0.01). Steroid dose could be reduced after intravenous immunoglobulin (IVIg) (p less than 0.05). Further research is needed. The level of evidence for PM is Category 2a - Evidence of probable benefit - more research needed. **Dermatomyositis (DM):** The Biotext (2004) review identified one double-blind, placebo-controlled trial considered of low quality of 15 patients with biopsy-confirmed, treatment-resistant DM. IVIg treatment combined with prednisone led to significant improvement in muscle strength and neuromuscular symptoms of patients in the intervention group (n = 8). One retrospective chart review and two case series tried IVIg as add on therapy (Class III evidence). Taken together, 82 percent improved clinically in these studies. The level of evidence for DM is Category 2a - Evidence of probable benefit - more research needed. **Necrotising autoimmune myopathy (NAM):** Patients with NAM were likely to have previously been regarded as having PM, increasingly this is being recognised as a separate entity. Small-case series consistently report improvement with immunosuppressive therapy. Often multiple immunotherapeutic agents are required. High-dose steroids are the mainstay of therapy, with IVIg required for some months as rescue therapy in some patients, until other immunosuppressive agents become effective. No trials of IVIg or prospective series have been

	conducted in NAM. Further research is needed. The level of evidence for NAM is Category 4a - Small case studies only, insufficient data.
Diagnosis Requirements	A diagnosis must be made by an Immunologist, Neurologist or a Rheumatologist.

Qualifying Criteria for Ig Therapy	• In adults, biopsy-proven PM, DM or NAM; or in children, diagnostic muscle biopsy or demonstration of the following three characteristics:
	  ◦ characteristic rash;
	  ◦ elevated muscle enzymes;
	  ◦ typical MRI scan abnormalities
	
	AND
	
	• Significant muscle weakness, as measured in an adult by a Medical Research Council (MRC) sum score of 55 points or less; or in a child by the Childhood Myositis Assessment Scale (CMAS) to a value of 44 points or less
	
	OR
	
	• Significant dysphagia limiting dietary intake with involvement of pharyngeal muscles as demonstrated by video-fluoroscopy unless speech pathology assessment indicates that video fluoroscopy in the particular patient is associated with an unacceptable risk of aspiration
	
	AND
	
	• Unresponsive to corticosteroid treatment
	
	OR
	
	• Unable to tolerate corticosteroids due to unacceptable side effects or significant toxicity
	
	OR
	
	• Corticosteroid therapy is contraindicated
	
	AND
	
	• At least two immunosuppressant agents (one of which should be corticosteroids) have been used and are ineffective or have been commenced but not yet become effective
	
	OR
	
	• Immunosuppressant medication is contraindicated
	
	IVIg should be used for up to four months (induction plus three maintenance cycles) before determining whether the patient has responded. If there is no benefit after this treatment, IVIg therapy should be abandoned.
	
	Review by a neurologist, rheumatologist, or immunologist is required within four months and annually thereafter. Cessation of Ig therapy should be considered at each review once stable or when alternative immunosuppressant agents have been commenced and are effective and the patient is stable.
	
	Documentation of clinical efficacy is necessary for continuation of Ig therapy.

Exclusion Criteria	Inclusion body myositis (IBM) - see Inclusion Body Myositis (IBM)

Review Criteria for Assessing the Effectiveness of Ig Use

IVIg should be used for up to four months (induction plus three maintenance cycles) before determining whether the patient has responded. If there is no benefit after this treatment, IVIg therapy should be abandoned.

Review by a neurologist, rheumatologist, or immunologist is required within four months and annually thereafter. Cessation of Ig therapy should be considered at each review once stable or when alternative immunosuppressant agents have been commenced and are effective and the patient is stable.

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

Clinical effectiveness of Ig therapy may be assessed by:

On review of the initial authorisation period

- Improvement in muscle weakness compared to the qualifying assessment as measured in adults by an increase in the Medical Research Council (MRC) sum score; or in children by an increase in the Childhood Myositis Assessment Scale (CMAS) score of at least two points

  OR

- Improvement in symptoms of dysphagia compared to the qualifying assessment as assessed by speech pathology, tolerance of food textures and/or reduced episodes of aspiration

On review of a continuing authorisation period

- Stabilisation or continued improvement in muscle weakness and symptoms as measured by the Medical Research Council (MRC) sum score or Childhood Myositis Assessment Scale (CMAS) score greater than or equal to the previous review score

  OR

- Patient with severe disease continues to report post infusion improvement with end-of-cycle deterioration and additional immunosuppressant agents have been commenced

  OR

- Stabilisation of, or continued improvement in symptoms of dysphagia compared to the previous review assessment as measured by speech therapy, improved tolerance of food texture and/or reduced episodes of aspiration

AND

- A trial of Ig weaning towards cessation of Ig therapy is planned for patients who are clinically stable to identify those in remission or a reason provided as to why a trial is not planned

For stable patients on maintenance treatment, review by a specialist is required at least annually. Most patients do not require long term therapy and progressive reduction in dosing should be considered.

Cessation of Ig therapy should be considered once alternative immunomodulating agents have been commenced and are effective and the patient is stable.

Dose	• **Induction Dose (IVIg)** - 2 g/kg in 2 to 5 divided doses. • **Maintenance Dose (IVIg)** - 0.4–1 g/kg, 4–6 weekly. A maximum total dose of 1g/kg may be given in any four week period. This can be administered in weekly divided doses, provided the total maximum is not exceeded. Most patients do not require long term therapy and progressive reduction in dosing should be considered. Cessation of Ig therapy should be considered once alternative immunomodulating agents have been commenced and are effective and the patient is stable. 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.

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