Cicatricial pemphigoid (CP) or Mucous Membrane Pemphigoid (MMP)

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Condition for which IVIg has an emerging therapeutic role.

Specific Conditions	• Cicatricial pemphigoid (CP) • Mucous Membrane Pemphigoid (MMP)
Indication for IVIg Use	• Cicatricial pemphigoid (CP) / Mucous Membrane Pemphigoid (MMP) resistant to corticosteroid and immunosuppressant therapy, or when these agents are contraindicated
Level of Evidence	Evidence of probable benefit – more research needed (Category 2a)
Description and Diagnostic Criteria	Cicatricial pemphigoid (CP) or Mucous Membrane Pemphigoid (MMP) is a rare, acquired subepithelial blistering disease characterised by erosive lesions of mucous membranes and skin. It is associated with autoantibodies to antigenic proteins in the epidermal basement membrane. Serious complications may occur due to erosions and scarring of affected tissues. Nasopharyngeal or laryngeal involvement may cause hoarseness, pain, tissue loss and even upper airway destruction, and oesophageal and urogenital lesions may lead to stenosis or strictures. CP/MMP is usually a chronic, progressive disorder. The aim of long-term treatment is cessation of the autoimmune process. Failure to do so results in invariable progression of the disease, culminating in progressive scarring. Permanent remission is usually possible if the disease is diagnosed early and treated sufficiently for one to five years. For the 70 percent of patients who have eye involvement, the disease progresses to conjunctival scarring and shrinkage, but may take 10 to 20 years to reach the end stage of bilateral blindness.
Justification for Evidence Category	A review of case reports and reports on small series of patients published in 2012 identified 72 patients who had received IVIg therapy for Cicatricial pemphigoid (CP) or Mucous Membrane Pemphigoid (MMP) (Czernik A et al, 2012). The majority of patients experienced an improvement of disease manifestations and a decline in serum levels of autoantibodies to epidermal basement membrane antigens, where examined. Disease remissions for at least 12 months were common. Doses of IVIg given were usually higher than used for other autoimmune diseases, at 2-3g/kg over three to five days every two weeks, because CP/MMP that is unresponsive to steroids and immunosuppressant therapy may cause considerable disability, particularly blindness from conjunctival ulceration and oesophageal strictures from oesophageal ulceration. Preliminary data suggest that a combination of IVIg and therapeutic B cell depletion through the use of rituximab arrests disease progression and prevents blindness in patients with conjunctival involvement that is unresponsive to corticosteroid and immunosuppressant therapy (Foster CS et al, 2010).
Diagnosis Requirements	A diagnosis must be made by an Immunologist, Dermatologist or an Ophthalmologist.

Qualifying Criteria for IVIg Therapy	• Moderate to severe CP/MMP disease with involvement of multiple sites, oesophageal involvement alone or conjunctiva alone, confirmed by biopsy or demonstration of autoantibodies AND • Unresponsive to standard corticosteroid and immunosuppressant therapy (using steroids and at least two alternative medications or Rituximab) OR • Corticosteroid and immunosuppressant medication are contraindicated or have resulted in unacceptable side effects or significant toxicity Review is required every six months by a dermatologist or ophthalmologist or immunologist. Response must be demonstrated at the initial review at six months and improvement must be demonstrated for continuation of supply. Dosing should be reduced progressively and consideration should be given to a trial-off immunoglobulin (Ig) therapy once the patient has achieved stabilised disease or clinical remission.
Review Criteria for Assessing the Effectiveness of IVIg Use	Review is required every six months by a dermatologist or ophthalmologist or immunologist. Response must be demonstrated at the initial review at six months and improvement must be demonstrated for continuation of supply. Dosing should be reduced progressively and consideration should be given to a trial off immunoglobulin (Ig) therapy once the patient has achieved stabilised disease or clinical remission. **Clinical effectiveness of Ig therapy may be assessed by:** **On review of the initial authorisation period** • A reduction in the number and severity of lesions compared to the qualifying assessment **On review of a continuing authorisation period** • A reduction in the number and severity of lesions compared to the previous review or the disease has stabilised AND • A trial of weaning towards cessation of Ig therapy is planned for patients who are clinically stable or a reason is provided as to why a trial is not planned

Dose	
	• **Maintenance Dose** - Initial treatment at 2g/kg to gain control and reducing to the lowest dose that still adequately controls disease. A maximum of 3 g/kg in any four week period with two weekly dosing supported where eyesight is threatened. Dosing should be reduced progressively and consideration should be given to a trial-off immunoglobulin (Ig) therapy once the patient has achieved stabilised disease or clinical remission. 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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