Pemphigus vulgaris (PV)

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Condition for which IVIg has an emerging therapeutic role.

Specific Conditions	• Pemphigus vulgaris
Indication for IVIg Use	• Moderate to severe PV as an adjuvant to prolonged corticosteroid and immunosuppressant treatment, or when these agents are contraindicated
Level of Evidence	Evidence of probable benefit – more research needed (Category 2a)
Description and Diagnostic Criteria	Pemphigus vulgaris (PV) is a rare but potentially fatal condition accounting for approximately 70 percent of pemphigus cases. While the cause is unknown, an immunogenetic predisposition is well established. PV may also be drug-induced. Drugs reported to be most significantly associated with PV include penicillamine, captopril and other thiol-containing compounds. Rifampicin and emotional stress have recently been reported as triggers for PV. The oral cavity is almost always affected and erosions can be scattered and extensive, with subsequent dysphagia. Blistering and erosions secondary to the rupture of blisters may be painful and limit the patient's daily activities. Pemphigus may occur in patients with other autoimmune diseases, particularly myasthenia gravis and thymoma. **Prognosis** The severity and natural history of PV are variable. Before the advent of steroids, most patients with PV died. Treatment with systemic steroids has reduced the mortality rate to five to 15 percent. Most deaths occur during the first few years of disease and, if the patient survives five years, the prognosis is good. Early disease is easier to control than widespread disease, and mortality may be higher if therapy is delayed. Morbidity and mortality are related to the extent of disease, the maximum dose of corticosteroid required to induce remission, and the presence of other diseases.
Justification for Evidence Category	In a retrospective cohort study, 15 corticosteroid-dependent patients with moderate to severe Pemphigus vulgaris (PV) were treated with intravenous immunoglobulin (IVIg) and followed over a mean period of 6.2 years. All 15 patients had a satisfactory clinical response to IVIg therapy. IVIg had a demonstrable corticosteroid sparing effect and was considered a safe and effective alternative treatment in patients who were dependent on systemic corticosteroids or who developed significant adverse effects as a result of their use (Biotext 2004). In a 2009 (Amagai et al 2009) small randomised controlled trial for pemphigus vulgaris and foliaceus patients (61 patients in total) demonstrated both Ig safety and efficacy when used at 0.4 g/kg for five days monthly.
Diagnosis Requirements	A diagnosis must be made by an Immunologist or a Dermatologist.

Qualifying Criteria for IVIg Therapy	• Moderate to severe PV disease, including widespread oral lesions, laryngeal involvement and/or erosions in skinfolds (vegetans) 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 agents are contraindicated or have resulted in unacceptable side effects or significant toxicity Review is required every six months by a dermatologist or immunologist 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 clinical remission.
Review Criteria for Assessing the Effectiveness of IVIg Use	Review is required every six months by a dermatologist or immunologist 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 clinical remission. **Clinical effectiveness of Ig therapy may be demonstrated 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 previous review, but active disease persists AND • A trial of weaning/ cessation of Ig therapy is planned for patients who are clinically stable or a reason is provided as to why a trial-off is not planned
Dose	• **Maintenance Dose** - 2g/kg per month. Dosing should be reduced progressively and consideration should be given to a trial-off immunoglobulin (Ig) therapy once the patient has achieved 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.

Bibliography

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