Specialist Working Group for Immunology

Proposed changes to the *Criteria for the clinical use of intravenous immunoglobulin in Australia, Second Edition*

ITEM	CRITERIA FOR THE CLINICAL USE OF INTRAVENOUS IMMUNOGLOBULIN IN AUSTRALIA, SECOND EDITION	PROPOSED REVISIONS TO THE CRITERIA	SWG RATIONALE FOR PROPOSED CHANGE (A) Administrative) (B) Progressive (C) Programmed
Condition Name	**Pemphigus foliaceus (PF)**	**Pemphigus foliaceus (PF)**	
Specialty	Dermatology	Dermatology	
Chapter	6	6	
Specific Conditions		Pemphigus erythematosus Pemphigus herpetiformis Endemic pemphigus foliaceus IgA pemphigus foliaceus Paraneoplastic pemphigus foliaceus Drug-induced pemphigus foliaceus	Specialist Working Group (SWG) and College of Dermatology recommend that these specific conditions are eligible. (A)
Description and Diagnostic Criteria	PF is a rare autoimmune blistering skin disease characterised by loss of cohesion of cells (acantholysis) in the superficial (subcorneal) layers of the epidermis. The lesions are generally well demarcated and do not coalesce to form large eroded areas (as seen in pemphigus vulgaris). It is mediated by an autoantibody that targets desmoglein 1, a cell-to-cell protein molecule that binds the desmosomes of neighbouring keratinocytes in the epidermis. The disease has a long-term course with patients	PF is a rare autoimmune blistering skin disease characterised by loss of cohesion of cells (acantholysis) in the superficial (subcorneal) layers of the epidermis. The lesions are generally well demarcated and do not coalesce to form large eroded areas (as seen in pemphigus vulgaris). It is mediated by an autoantibody that targets desmoglein 1, a cell-to-cell protein molecule that binds the desmosomes of neighbouring keratinocytes in the epidermis. The disease has a long-term course with	Unchanged.

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	maintaining satisfactory health. Spontaneous remissions occasionally occur.	patients maintaining satisfactory health. Spontaneous remissions occasionally occur.			
Level of Evidence	Small case studies only; insufficient data (Category 4a).	Evidence of probable benefit – more research needed. (Category 2a).			SWG and College of Dermatology recommend that level of evidence should be changed to Category 2a. (A)
Justification for Evidence Category	Habif (2004) concluded that IVIg was effective as monotherapy for PF and particularly useful in patients who experienced life-threatening complications from immunosuppression. Sami et al (2002) observed that autoantibody titres to desmoglein 1 in a series of 15 PF patients declined persistently following IVIg therapy.	Habif (2004) concluded that intravenous immunoglobulin (IVIg) was effective as monotherapy for PF and particularly useful in patients who experienced life-threatening complications from immunosuppression. Sami et al (2002) observed that autoantibody titres to desmoglein 1 in a series of 15 PF patients declined persistently following IVIg therapy. Amagai M et al conducted a small randomised controlled trial (RCT) in 2009 for pemphigus vulgaris and foliaceus patients (61patients in total) that supported both safety and efficacy of Ig therapy.			This section was reviewed and revised. A small RCT was added supporting a change in evidence level. (A)
Diagnosis is required	Severe widespread PF, defined as disease involving 30% or more of body surface area, diagnosed by a dermatologist;	Yes	Which Speciality	Dermatologist Immunologist	Unchanged
Diagnosis must be verified		No	Which Specialty		
Exclusion Criteria					
Indication for use	PF resistant to corticosteroids and immunosuppressive therapy or when these agents are contra-indicated.	**PF resistant to corticosteroids and immunosuppressive therapy or when these agents are contraindicated.**			Unchanged

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Qualifying Criteria	Severe widespread PF, defined as disease involving 30% or more of body surface area, diagnosed by a dermatologist; AND 1. Corticosteroids or immunosuppressive agents are contraindicated; OR 2. Condition is unresponsive to corticosteroids and immunosuppressive agents; OR 3. Presenting with severe side effects of therapy.	• Severe widespread proven PF disease involving at least 30% body surface, positive direct immunofluorescence test and autoantibody titre AND • Persistent disease despite standard corticosteroid and immunosuppressant therapy using Rituximab or two alternative immunosuppressant agents. OR • Persisant disease and severe side effects prohibit the continuation of corticosteroids and immunosuppressant agents. OR • Persistant disease and corticosteroids and/or immunosuppressant agents are contraindicated.	Qualifying criteria requiring confirmation of diagnosis and evidence items to be tracked to determine response have been defined. (A) Options for immunosuppressive therapy are i. Corticosteroids ii. Azathioprine iii. Methotrexate iv. Mycophenolate v. Rituximab Values for severe immunosuppressant side effects include i. Significant infection including sepsis ii. Malignancy iii. Marrow suppression and cytopenia iv. Unstable Diabetes v. Severe osteoporosis vi. History of avascular necrosis (A)
Review Criteria	• Response demonstrated at review at six months. Improvement to be demonstrated for continuation of supply. • Clinical progression: Treatment is stopped when patients are clinically free from disease and have a negative finding on direct	Review is required every six months by a Dermatologist and improvement must be demonstrated for continuation of supply. Autoantibody titres reflect the response to systemic therapy. **On review of an authorisation period**	Review criteria and evidence items have been defined. (A)

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	immunofluorescence. • Autoantibody titres reflect the response to systemic therapy.	• Response to immunoglobulin (Ig) therapy is demonstrated by a reduced percentage of body surface area affected compared to the qualifying value. AND • The autoantibody titre is reduced. AND • Patients qualify for further treatment if the direct immunofluorescence test remains positive. Clinical progression: treatment is stopped when patients are clinically free from disease and have a negative finding on direct immunofluorescence.	Review is conducted six monthly. Autoantibody Titre is a direct correlator to disease severity, but more so as a marker for control of disease with treatment. Cessation of treatment is defined. (A)
Dose	Efficacy demonstrated with doses of at least 2 g/kg per monthly treatment cycle. **Dosing above 1 g/kg per day is contraindicated for some IVIg products.** **Refer to the current product information sheet for further information.** **The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for**	**Maintenance** - Efficacy demonstrated with doses of at least 2 g/kg per monthly treatment cycle. The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient Dosing above 1 g/kg per day is contraindicated for some IVIg products. **Refer to the current product information sheet for further information.**	Dosing unchanged

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	each patient.		

BIBLIOGRAPHY

Habif TP. Vesicular and bullous diseases. Chapter 16 in: Clinical Dermatology [electronic resource] : A Color Guide to Diagnosis and Therapy, 4th edition. Mosby Inc, Edinburgh. 2004

Sami, N, Bhol, KC & Razzaque, A 2002, 'Influence of IVIg therapy on autoantibody titres to desmoglein 1 in patients with pemphigus foliaceus', *Clinical Immunology,* vol. 105, no. 2 pp. 192–8.

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