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 (CRITERIA)	PROPOSED REVISIONS TO THE CRITERIA (INCLUDING ADAPTATION TO THE IG SYSTEM)	SWG RATIONALE FOR PROPOSED CHANGE (A) Administrative) (B) Progressive (C) Programmed
Condition Name	**Bullous pemphigoid (BP)**	**Bullous pemphigoid (BP)**	
Specialty	Dermatology	Dermatology	
Chapter	6	6	
Specific Conditions			
Level of Evidence	Small case studies only; insufficient data (Category 4a).	Evidence of probable benefit from cases studies and small case series (Category 2a).	Specialist Working Group and College of Dermatology recommends changing the level of evidence from 4a to 2a. (A)
Justification for Evidence Category	The 2003 Harvard consensus statement identified a small study (17 cases) where patients who were on IVIg therapy for at least three months benefited from the therapy. The same article mentioned another small study (15 cases) where patients with BP could not be controlled with high-dose systemic corticosteroids and multiple immunosuppressive agents. IVIg produced prolonged clinical remission sustained after IVIg therapy was discontinued.	The 2003 Harvard consensus statement (Ahmed and Dahl 2003) identified a small study (17 cases) where patients who were on intravenous immunoglobulin (IVIg) therapy for at least three months benefited from the therapy. The same article mentioned another small study (15 cases) where patients with BP could not be controlled with high-dose systemic corticosteroids and multiple immunosuppressive agents. IVIg produced prolonged clinical remission sustained after IVIg therapy was discontinued. In 2012, a published small case series (including pooled case reviews from literature), reported that approximately 75% of patients with BP responded to IVIg treatment, especially when used early on in the	Section was revised and additional small case series were added demonstrating benefit when used early on in the course of disease. (A)

ITEM	CRITERIA FOR THE CLINICAL USE OF INTRAVENOUS IMMUNOGLOBULIN IN AUSTRALIA, SECOND EDITION (CRITERIA)	PROPOSED REVISIONS TO THE CRITERIA (INCLUDING ADAPTATION TO THE IG SYSTEM)	SWG RATIONALE FOR PROPOSED CHANGE (A) Administrative) (B) Progressive (C) Programmed
		course of disease.	
Description and Diagnostic Criteria There should be no change the published text	BP is a rare disease of elderly people characterised by tense blisters and vesicles with a prominent inflammatory component. The cause is unknown. Lesions result from a failure of basal keratinocytes to adhere to the epidermal basement membrane. The course of BP is characterised by exacerbations and remissions. Pruritis is a common feature and an increase in pruritis may herald an exacerbation. In most patients, BP is not a life-threatening disease. The side effects of systemic immunosuppressive therapy need to be managed. In most patients, the disease spontaneously clears within six years and all medication can be stopped. In a small group, the disease recurs after treatment is stopped. Skin infection is the most common complication. A submission by the Australasian College of	BP is a rare disease of elderly people characterised by tense blisters and vesicles, with a prominent inflammatory component. The cause is unknown. Lesions result from a failure of basal keratinocytes to adhere to the epidermal basement membrane. The course of BP is characterised by exacerbations and remissions. Pruritis is a common feature and an increase in pruritis may herald an exacerbation. In most patients, BP is not a life-threatening disease. The side effects of systemic immunosuppressive therapy need to be managed. In most patients, the disease spontaneously clears within 2-3 years and all medication can be stopped. In a small group, the disease recurs after treatment is stopped. Skin infection is the most common complication. A submission by the Australasian College of Dermatologists recommends IVIg use in BP only in severe cases where improvement with conventional therapy is not readily achieved.	College of Dermatology recommended to change period for spontaneous clearance of disease from 6 to 2-3 years. (A)

ITEM	CRITERIA FOR THE CLINICAL USE OF INTRAVENOUS IMMUNOGLOBULIN IN AUSTRALIA, SECOND EDITION (CRITERIA)	PROPOSED REVISIONS TO THE CRITERIA (INCLUDING ADAPTATION TO THE IG SYSTEM)			SWG RATIONALE FOR PROPOSED CHANGE (A) Administrative) (B) Progressive (C) Programmed
	Dermatologists recommends IVIg use in BP only in severe cases where improvement with conventional therapy is not readily achieved.				
Diagnosis is required		Yes	Which Speciality	Dermatologist or Clinical Immunologist	Clinical Immunologist added to the specialist list to able to prescribe as they were often consulted and ordered the Ig. (A)
Diagnosis must be verified		No	Which Specialty		
Exclusion Criteria					
Indications	BP resistant to topical and systemic glucosteroids and immunosuppressive therapy.	**BP resistant to topical and systemic glucocorticoids and immunosuppressive therapy**			Indication reworded slightly (A)
Qualifying Criteria	Moderate to severe disease diagnosed by a dermatologist AND 1. Corticosteroids or immunosuppressive agents are contraindicated; OR 2. Condition is unresponsive to corticosteroids and immunosuppressive	• Moderate to severe BP disease confirmed by blood testing and biopsy AND • Persistent disease despite standard corticosteroid and immunosuppressant therapy (using steroids and at least two alternative medications or rituximab) OR • Persistant disease and severe side effects prohibit the continuation of corticosteroids and			Qualifying criteria and evidence items are defined including diagnostic requirements to be confirmed by biopsy and blood testing. (A) Alternative therapies to Ig include: i. Corticosteroids ii. Azathioprine iii. Methotrexate iv. Mycophenolate v. Rituximab Severe immunosuppressant side effects include: i. Significant infection including sepsis

ITEM	CRITERIA FOR THE CLINICAL USE OF INTRAVENOUS IMMUNOGLOBULIN IN AUSTRALIA, SECOND EDITION (CRITERIA)	PROPOSED REVISIONS TO THE CRITERIA (INCLUDING ADAPTATION TO THE IG SYSTEM)	SWG RATIONALE FOR PROPOSED CHANGE (A) Administrative) (B) Progressive (C) Programmed
	agents; OR 3. Presenting with severe side effects of therapy.	immunosuppressant agents OR • Persistant disease and corticosteroids or immunosuppressant agents are contraindicated.	ii. Malignancy iii. Marrow suppression and cytopenia iv. Unstable Diabetes v. Severe osteoporosis vi. History of avascular necrosis Contraindication Reasons 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. • Reduction in recurrence of disease or relapse. • Ability to reduce dose or discontinue other therapies. • Improved quality of life. • Resolution of blisters and healing of affected skin.	Review is required every six months by a dermatologist or clinical immunologist. Response must be demonstrated at the initial review at six months and improvement must be demonstrated for continuation of supply. Consideration should be given to a trial-off immunoglobulin (Ig) therapy once the patient has achieved stabilised disease or clinical remission. The minimal effective dose should be prescribed. **On review of an initial authorisation period** • Response has been demonstrated by a reduction in the number and severity of lesions compared	Review criteria and evidence items have been defined. Review will be undertaken every 6 months and a trial off therapy prompted for. (A) If continuing Ig treatment, a reduction in the dose is requested. (A)

ITEM	CRITERIA FOR THE CLINICAL USE OF INTRAVENOUS IMMUNOGLOBULIN IN AUSTRALIA, SECOND EDITION (CRITERIA)	PROPOSED REVISIONS TO THE CRITERIA (INCLUDING ADAPTATION TO THE IG SYSTEM)	SWG RATIONALE FOR PROPOSED CHANGE (A) Administrative) (B) Progressive (C) Programmed
	• Resolution of pruritis.	to qualifying with more than 30% improvement to be achieved. **On review of a continuing authorisation period** • Response has been demonstrated by a reduction in the number and severity of lesions compared to the previous review, but there is remaining activity or stable disease. AND • A trial-off Ig therapy is planned or the reason why a trial is not planned is provided. AND • If continuing Ig therapy, a reduction in dose is planned or, if not planned, a reason is provided.	
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**	**Maintenance** - Efficacy demonstrated with doses of up to 2 g/kg per month. Consideration should be given to a trial-off immunoglobulin (Ig) therapy once the patient has achieved stabilised disease or clinical remission. The minimal effective dose should be prescribed. The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.	The dosing description has been revised to describe doses up to 2g/kg rather than at least 2g/kg. Dosing is encouraged to be reduced progressively and Ig therapy ceased once disease has stabilised. (A)

ITEM	CRITERIA FOR THE CLINICAL USE OF INTRAVENOUS IMMUNOGLOBULIN IN AUSTRALIA, SECOND EDITION (CRITERIA)	PROPOSED REVISIONS TO THE CRITERIA (INCLUDING ADAPTATION TO THE IG SYSTEM)	SWG RATIONALE FOR PROPOSED CHANGE (A) Administrative) (B) Progressive (C) Programmed
	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.**	

BIBLIOGRAPHY

Ahmed, AR & Dahl, MV, for the Consensus Development Group 2003, 'Consensus statement on the use of intravenous immunoglobulin therapy in the treatment of autoimmune mucocutaneous blistering diseases', *Archives of Dermatology,* vol. 139, pp. 1051–9.

Gaitanis, G, Alexis, I, Pelidou, SH, et al 2012, 'High-dose intravenous immunoglobulin in the treatment of adult patients with bullous pemphigoid', European Journal of Dermatology, vol. 22, no. 3, pp. 363–9.

Orange, JS, Hossny, EM, Weiler, CR, et al 2006, 'Use of intravenous immunoglobulin in human disease: A review of primary evidence by members of the Primary Immunodeficiency Committee of the American Academy of Allergy, Asthma and Immunology', *Journal of Allergy and Clinical Immunology*, vol. 117, no. 4, pp. S525–53.

END OF DOCUMENT