Specialist Working Group for Haematology

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, EDITION 2	PROPOSED REVISIONS TO THE CRITERIA	SWG RATIONALE FOR PROPOSED CHANGE (A) Administrative) (B) Progressive (C) Programmed
Condition Name	**Haemophagocytic syndrome**	**Haemophagocytic syndrome**	
Specialty	Haematology	Haematology	Haemophagocytic syndrome
Chapter	6	6	
Specific Conditions			
Level of Evidence	Small case studies only; insufficient data (Category 4a).	Small case studies only; insufficient data (Category 4a).	
Justification for Evidence Category	No RCTs have been done, although many, mostly small, case series show evidence of benefit.	No randomised controlled trials (RCTs) have been done, although many, mostly small, case series show evidence of benefit.	
Description and Diagnostic Criteria	Haemophagocytic syndrome is characterised by fever, splenomegaly, jaundice, rash and the pathologic finding of haemophagocytosis (phagocytosis by macrophages of erythrocytes, leukocytes, platelets and their precursors) in bone marrow and other tissues with peripheral blood cytopenias. Haemophagocytic syndrome has been associated with a wide range of infectious, autoimmune,	Haemophagocytic syndrome is characterised by fever, splenomegaly, jaundice, rash and the pathologic finding of haemophagocytosis (phagocytosis by macrophages of erythrocytes, leukocytes, platelets and their precursors) in bone marrow and other tissues with peripheral blood cytopenias. Haemophagocytic syndrome has been associated with a wide range of infectious, autoimmune, malignant and other disorders (modified from Fisman 2000). Mortality is high.	

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	malignant and other disorders (modified from Fisman 2000). Mortality is high.		
Diagnosis is required		No / Which Speciality	
Diagnosis must be verified		No / Which Specialty	
Exclusion Criteria		Children with hemophagocytic lymphohistiocytosis (HLH) and hypogammaglobulinaemia - see Secondary hypogammaglobulinaemia unrelated to haematological malignancy.	This indication is only for the treatment of severe refractory HPS. Ig therapy is recommended practice in current international protocols when children undergoing treatment with alternative medications become hypogammaglobulinaemic. This should be treated under secondary hypogammaglobulinaemia if children are eligible under that condition.
Indication for use	Management of severe haemophagocytic syndrome not responding to other treatments.	**Management of severe haemophagocytic syndrome not responding to other treatments~~.~~**	Unchanged
Qualifying Criteria	Bone marrow diagnosis or other biopsy evidence of haemophagocytosis in the characteristic clinical setting. **Note:** Since other therapies (cytotoxic agents) have major potential side effects, optimal therapy is not yet defined.	• Bone marrow diagnosis or other biopsy evidence of haemophagocytosis. AND • Clinical features characteristic of haemophagocytic syndrome. AND • Non-response or ineligibility for other treatments.	Qualifying criteria are consistent with current criteria Addition of requirement for non response to other therapies and ineligibility for other treatments. Script deleted as not seen to be helpful and non response to other treatments is a qualifying criteria.

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Review Criteria	Amelioration of cytopenia(s), hepato/splenomegaly and lymphadenopathy if present. Survival or death.	Review is not mandated for this indication however the following criteria may be useful in assessing the effectiveness of therapy. **Outcome data to be measured** Review criteria for assessing the effectiveness of IVIg use can be demonstrated by: • Survival and improvement in: o cytopoenia(s) o hepatosplenomegaly o lymphadenopathy (if present) o neurologic abnormalities.	Outcome data are defined.
Dose	2 g/kg is the most widely published dose. Emmenegger et al (2001) reported that better outcomes were associated with early administration of IVIg in their small case series (10 patients). 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	**Induction Dose** - 2 g/kg is the most widely published dose. Emmenegger et al (2001) reported that better outcomes were associated with early administration of IVIg in their small case series (10 patients). 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 is unchanged.

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	contraindicated for some IVIg products. **Refer to the current product information sheet for further information.**		

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