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	**Kawasaki disease (mucocutaneous lymph node syndrome)**	**Kawasaki disease (mucocutaneous lymph node syndrome)**	
Specialty		Immunology	
Chapter	5	5	
Specific Conditions			
Level of Evidence	Clear evidence of benefit (Category 1).	Clear evidence of benefit (Category 1).	
Justification for Evidence Category	One high-quality systematic review of 16 RCTs that showed that IVIg is of benefit in treating Kawasaki disease (Biotext 2004).	One high-quality systematic review of 16 randomised controlled trials (RCTs) that showed that IVIg is of benefit in treating Kawasaki disease (Biotext 2004).	Unchanged
Description and Diagnostic Criteria	Kawasaki disease is an acute, febrile, multi-system disease of children and young infants often involving the coronary arteries. Coronary artery aneurysms may occur from the second week of illness during the convalescent stage. The cause of the condition is unknown but there is evidence that the characteristic vasculitis results from an immune reaction characterised by T-cell and macrophage activation to an	Kawasaki disease is an acute, febrile, multi-system disease of children and young infants, often involving the coronary arteries. Coronary artery aneurysms may occur from the second week of illness during the convalescent stage. The cause of the condition is unknown, but there is evidence that the characteristic vasculitis results from an immune reaction characterised by T-cell and macrophage	Updated to address revised diagnostic criteria when there is cardiac involvement. (A)

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	unknown antigen, secretion of cytokines, polyclonal B-cell hyperactivity, and the formation of autoantibodies to endothelial cells and smooth muscle cells. It is likely that in genetically susceptible individuals, one or more uncharacterised common infectious agents, possibly with super-antigen activity, may trigger the disease. **Diagnosis** A diagnosis of Kawasaki disease is generally made if fever of four or more days' duration is associated with at least four of the following changes, which often appear sequentially: • bilateral (non-purulent) conjunctival injection; • changes of the mucous membranes of the upper respiratory tract and oropharynx, including diffuse redness of pharyngeal mucosa, dry fissured lips, red fissured lips, and/or 'strawberry tongue'; • changes of the extremities, including peripheral erythema, peripheral oedema, and subsequent periungual or more generalised desquamation; • polymorphous rash;	activation to an unknown antigen, secretion of cytokines, polyclonal B-cell hyperactivity, and the formation of autoantibodies to endothelial cells and smooth muscle cells. It is likely that in genetically susceptible individuals, one or more uncharacterised common infectious agents, possibly with super-antigen activity, may trigger the disease. **Diagnosis** A diagnosis of Kawasaki disease is generally made if fever of four or more days' duration is associated with at least four of the following changes, which often appear sequentially, or three if coronary abnormalities are evident on echocardiogram: • bilateral (non-purulent) conjunctival injection • changes of the mucous membranes of the upper respiratory tract and oropharynx, including diffuse redness of pharyngeal mucosa, dry fissured lips, red fissured lips, and/or 'strawberry tongue' • changes of the extremities, including peripheral erythema, peripheral oedema, and subsequent periungual or	

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	• cervical lymphadenopathy. A diagnosis of Kawasaki disease may be made if fever and fewer than four of the changes listed above are present where there is strong clinical suspicion of Kawasaki disease (refer to Newburger 2004). Between 10% and 20% of cases, particularly in younger infants, present with fever and fewer than four of the listed criteria. Expert advice should be sought. Data support the use of IVIg while there is ongoing inflammation (usually taken as ongoing fever or raised acute inflammatory markers). Prognosis is worse if IVIg is used 10 days post-onset, but should be used at any time if there is evidence of inflammation. Up to 15% of patients do not respond to initial IVIg therapy. Consensus is for re-treatment with 2 g/kg of IVIg before considering steroids.	more generalised desquamation • polymorphous rash • cervical lymphadenopathy. A diagnosis of Kawasaki disease may be made if fever and fewer than four of the changes listed above are present where there is strong clinical suspicion of Kawasaki disease (refer to Newburger 2004). Between 10% and 20% of cases, particularly in younger infants, present with fever and fewer than four of the listed criteria. Expert advice should be sought. Data support the use of intravenous immunoglobulin (IVIg) while there is ongoing inflammation (usually taken as ongoing fever or raised acute inflammatory markers). Prognosis is worse if IVIg is used 10 days post-onset, but should be used at any time if there is evidence of inflammation. Up to 15% of patients do not respond to initial IVIg therapy. Consensus is for re-treatment with 2 g/kg of IVIg before considering steroids.			
Diagnosis is required	Clinical diagnosis of Kawasaki disease by a paediatrician or immunologist.	Yes	Which Speciality	General paediatrician or immunologist or rheumatologist	Rheumatologist added as can be the treating specialist (A)
Diagnosis must be verified		No	Which Specialty		
Exclusion					

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Criteria			
Indications	Early Kawasaki Disease to prevent coronary artery pathology	**Early Kawasaki disease to prevent coronary artery pathology.** **Continued inflammation more than 36 hours after the initial dose of Ig therapy in early Kawasaki disease.**	Second indication added to provide controlled access to a second dose. (A)
Qualifying Criteria	Clinical diagnosis of Kawasaki disease by a paediatrician or immunologist.	**Early Kawasaki disease to prevent coronary artery pathology.** • A clinical diagnosis of Kawasaki disease has been made. Therapy should be initiated within 10 days of fever onset if possible; however, children who present after 10 days of fever still should be treated if fever or other signs of persistent inflammation are present. **Continued inflammation more than 36 hours after the initial Ig dose in early Kawasaki disease.** • A clinical diagnosis of Kawasaki disease has been made and treated with an initial dose of Ig therapy AND • There is evidence of ongoing inflammation at least 36 hours after the initial dose of Ig therapy, with	Qualifying criteria have been defined including evidence items for second dose. (A) Script added to educate prescribers and ensure patients are treated early, however, when late presentation, treatment should be given where fever or other signs of inflammation have persisted. (A)

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		persistent fever and/or ongoing elevated inflammatory markers.	
Review Criteria		Review is not mandated for this condition.	No useful outcome data was seen to be of value given that the condition already has level 1 evidence.
Dose	2 g/kg in a single dose over 10–12 hours unless cardiac function necessitates the administration of a prolonged or divided treatment dose, usually once only. Re-treatment with 2 g/kg in a single dose may be given when there is ongoing inflammation. **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 each patient.**	**Induction** - 2 g/kg in a single dose over 10–12 hours. **Induction dose with impaired cardiac function –** 2 g/kg in a divided dose. Dose Postscript Given over 10–12 hours, unless impaired cardiac function necessitates the administration of a prolonged or divided treatment dose, usually once only. Re-treatment with 2 g/kg in a single dose may be given when there is ongoing inflammation. 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 but reformatted with slight rewording regarding cardiac impairment (A)

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