Kawasaki disease (mucocutaneous lymph node syndrome)

Condition for which Ig has an established therapeutic role.

Specific Conditions	• Kawasaki disease
Indication for Ig Use	• Early Kawasaki disease to prevent coronary artery pathology
Level of Evidence	Clear evidence of benefit (Category 1)
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 dilatation, which may result in aneurysm formation, may be noted at presentation and most commonly occurs in the sub-acute phase of the illness, from day 10 onwards (onset of fever is day one). The cause of the condition is unknown, but there is evidence that the characteristic vasculitis results from an exaggerated pro-inflammatory immunological response that involves both the innate and adaptive arms of the immune system, characterised by T-cell and macrophage activation to an unknown antigen, secretion of cytokines, polyclonal B-cell hyperactivity. 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 cardinal diagnostic criteria, 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 more generalised desquamation, which occurs during the sub-acute phase; • 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 (Newburger et al 2004). Between 10 percent and 20 percent of cases, particularly in younger infants, present with fever and fewer than four of the listed criteria. Rarely, patients may also be shocked and have features of toxic shock syndrome, termed 'Kawasaki disease shock syndrome' (Lin et al 2015). 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 percent of patients do not respond to initial IVIg therapy. Consensus is for re-treatment with 2 g/kg of IVIg before considering steroids.
Justification for Evidence Category	One high-quality systematic review of 16 randomised controlled trials (RCTs) that showed that IVIg is of benefit in treating Kawasaki disease (Oates-Whitehead et al 2003).
Diagnosis Requirements	A diagnosis must be made by an Immunologist, Rheumatologist, Paediatrician, Intensivist, Paediatric Infectious Diseases Physician or a Cardiologist.
Qualifying Criteria for Ig Therapy	• Clinical diagnosis of Kawasaki disease 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 (including raised acute phase markers, such as CRP) of persistent inflammation are present.
Review Criteria for Assessing the Effectiveness of Ig Use	**Review is not mandated for this indication however the following criteria may be useful in assessing the effectiveness of therapy.** • Clinical response to Ig therapy

Dose	

- **Dose (IVIg)** - 2 g/kg in a single dose.
  Given over 10–12 hours, unless impaired cardiac function necessitates the administration of a prolonged treatment dose, usually once only. Re-treatment with 2 g/kg in a single dose may be given when there is ongoing inflammation more than 36 hours after initial Ig dose. Expert advice should be sought.

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 contraindication.

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