Autoimmune haemolytic anaemia (AIHA)

Version: 2.1
Published: 08 July 2016

Condition for which IVIg has an emerging therapeutic role.

Specific Conditions	• Autoimmune haemolytic anaemia
Indication for IVIg Use	• To reduce haemolysis in patients not responding to corticosteroid therapy or as a temporising measure before splenectomy. • As initial and maintenance therapy for AIHA in patients unsuitable for splenectomy or immunosuppression.
Level of Evidence	Insufficient data (Category 4a)
Description and Diagnostic Criteria	Autoimmune haemolytic anaemia (AIHA) is a rare but serious autoimmune disease in which an individual's antibodies recognise antigens on their own red blood cells. AIHA presents as an acute or chronic anaemia characterised by the occurrence of biochemical parameters of red cell destruction, associated with a positive direct antiglobulin test indicating the presence of antibodies and/or complement on the red cell surface. It may be secondary to a number of underlying disorders or drugs. **Investigations** A full blood count will confirm the presence of anaemia. A peripheral blood smear may reveal evidence of spherocytes along with polychromasia due to reticulocytosis. A direct antiglobulin test is usually positive, the serum lactate dehydrogenase is raised, and there is a reduction in serum haptoglobin. **Prognosis** The prognosis of AIHA is good in most cases, although severe refractory AIHA can cause cardio-respiratory problems because of severe anaemia, especially in adults. **Standard therapy** Corticosteroid administration is the cornerstone of therapy. For those with relapsing disease, splenectomy and immunosuppression are second-line treatments, while anti-CD20 antibodies have shown promise in individual cases of refractory disease.
Justification for Evidence Category	An analysis of 73 patients with AIHA in 1993, based on three pilot studies and a literature review, showed a 40% response to intravenous immunoglobulin (IVIg) given together with corticosteroids. A lower initial haemoglobin concentration and hepatomegaly were positive correlates of response. Several small case series have suggested a benefit for IVIg in AIHA associated with lymphoproliferative diseases, especially chronic lymphocytic leukaemia (CLL). On the basis of these findings, IVIg is not supported as standard therapy for AIHA. IVIg is only supported in cases refractory to conventional corticosteroid therapy, as a temporising measure before splenectomy, or as maintenance therapy where splenectomy or immunosuppression are not appropriate.

Qualifying Criteria for IVIg Therapy	To reduce haemolysis in patients not responding to corticosteroid therapy or as a temporising measure before splenectomy. • Symptomatic or severe disease (Hb <60 g/L, except in patients with co-morbidities) refractory to conventional therapy with corticosteroids. OR • Temporising measure before splenectomy. As initial and maintenance therapy for AIHA in patients unsuitable for splenectomy or immunosuppression. • Symptomatic or severe disease (Hb <60 g/L, except in patients with co-morbidities). AND • Haemolysis persists after a standard course of conventional corticosteroid therapy. OR • Corticosteroid therapy is contraindicated. AND • Splenectomy is contraindicated. OR • Immunosuppressant therapy is contraindicated.

Review Criteria for Assessing the Effectiveness of IVIg Use

To reduce haemolysis in patients not responding to corticosteroid therapy or as a temporising measure before splenectomy.

Review is not mandated for this indication however the following criteria may be useful in assessing the effectiveness of therapy.

Clinical effectiveness of Ig therapy may be demonstrated by:

- Improvement of signs and symptoms of haemolytic anaemia (rising haemoglobin concentrations, falling bilirubin and lactate dehydrogenase [LDH]).

As initial and maintenance therapy for AIHA in patients unsuitable for splenectomy or immunosuppression.

Review is required each 6 months for continuing treatment.

Documentation of clinical effectiveness is necessary for continuation of Ig therapy.

Corticosteroid administration is the cornerstone of therapy. For those with relapsing disease, splenectomy and immunosuppression are second-line treatments, while anti-CD20 antibodies have shown promise in individual cases of refractory disease.

On review of an authorisation request

Clinical effectiveness of Ig therapy may be demonstrated by:

- Improvement of haemolytic anaemia (rising haemoglobin concentrations, falling bilirubin and lactate dehydrogenase [LDH]).

Dose	To reduce haemolysis in patients not responding to corticosteroid therapy or as a temporising measure before splenectomy. • **Dose** - Up to 2g/kg, as a single dose or divided dose. Corticosteroid administration is the cornerstone of therapy. For those with relapsing disease, splenectomy and immunosuppression are second-line treatments, while anti-CD20 antibodies have shown promise in individual cases of refractory disease. **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.** As initial and maintenance therapy for AIHA in patients unsuitable for splenectomy or immunosuppression. • **Maintenance Dose** - 0.8–2 g/kg as a single or divided dose, 3 to 6 weekly. Corticosteroid administration is the cornerstone of therapy. For those with relapsing disease, splenectomy and immunosuppression are second-line treatments, while anti-CD20 antibodies have shown promise in individual cases of refractory disease. **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.**

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Generated on: 1 April 2019