Specific antibody deficiency (SAD)

Version: 2.1
Published: 07 July 2016

Condition for which IVIg has an emerging therapeutic role.

Specific Conditions	• Specific antibody deficiency • IgG subclass deficiency (existing authorisation)
Indication for IVIg Use	• Prevention of infections in individuals with frequent infections who have demonstrated failure to mount protective IgG antibody responses to vaccine antigen challenge, despite normal total serum IgG levels. • Life-threatening infection or a series of serious infections following trial-off Ig therapy in patients with proven specific antibody deficiency. • Patients currently receiving immunoglobulin therapy for a diagnosis of IgG subclass deficiency are eligible for continued therapy, but a diagnosis of specific antibody deficiency should be confirmed following cessation of immunoglobulin therapy.
Level of Evidence	Insufficient data (Category 4a)
Description and Diagnostic Criteria	The term 'specific antibody deficiency' describes failure of specific antibody response to an antigen challenge, and is most often used in the more restrictive sense of applying to polysaccharide antibody responses only. Patients who have normal total immunoglobulin G (IgG) levels but impaired production of specific antibodies, including those with isolated deficient responses to numerous polysaccharide antigens after vaccination, can present a diagnostic challenge. IgG replacement therapy should be provided when there is well-documented severe polysaccharide non-responsiveness and evidence of recurrent infections with a documented requirement for antibiotic therapy and ongoing recurrent infections despite antibiotic prophylaxis (Orange et al 2006). It is now generally agreed that IgG subclass level estimation in serum is relatively poorly predictive of infectious risk and is of limited value in the definition of those patients most likely to benefit from IVIg therapy. Further research investigating clinical and laboratory features of this disorder is required.
Diagnosis Requirements	A diagnosis must be made by any medical officer. Where the diagnosis was not made by an Immunologist the diagnosis must be verified by an Immunologist.
Qualifying Criteria for IVIg Therapy	Prevention of infections in individuals with frequent infections who have demonstrated failure to mount protective IgG antibody responses to vaccine antigen challenge, despite normal total serum IgG levels. • Documented failure of serum antibody response to conjugated or unconjugated pneumococcal vaccine or protein vaccine challenge. AND • Frequent and/or persistent and significant bacterial infections despite oral antibiotic therapy consistent with best practice recommendations.

	Life-threatening infection or a series of serious infections following trial-off Ig therapy in patients with proven specific antibody deficiency. • Patient with proven specific antibody deficiency undertaking a trial-off Ig therapy. Patients currently receiving immunoglobulin therapy for a diagnosis of IgG subclass deficiency are eligible for continued therapy, but a diagnosis of specific antibody deficiency should be confirmed following cessation of immunoglobulin therapy. • Existing patient on IgG therapy funded under the National Blood Arrangements in Australia. **Note**: IVIg is not funded for new patients diagnosed with IgG subclass deficiency.
Exclusion Criteria	Isolated IgG subclass deficiency in the absence of evidence of specific antibody deficiency. Low total IgG. This should be considered under primary or secondary immunodeficiency. - see Secondary hypogammaglobulinaemia (including iatrogenic immunodeficiency)

Review Criteria for Assessing the Effectiveness of IVIg Use

Prevention of infections in individuals with frequent infections who have demonstrated failure to mount protective IgG antibody responses to vaccine antigen challenge, despite normal total serum IgG levels.

Natural history of specific antibody deficiency remains poorly defined, although antibody production will improve for many patients over time, particularly children.

Review by a Clinical Immunologist required annually. Documentation of clinical effectiveness is necessary for continuation of Ig therapy.

Cessation of immunoglobulin therapy should be considered at least after each 12 months of Ig therapy, extended as required to enable cessation of therapy in September or October.

This should particularly be considered in patients who do not have active bronchiectasis and/or suppurative lung disease. An immunoglobulin washout period of four to six months is necessary to enable an accurate assessment. Prophylactic antibiotics may be considered to cover the period of cessation of immunoglobulin therapy.

Patients may qualify for further immunoglobulin therapy:

- under other immunodeficiency criteria (e.g. primary antibody deficiency disorder), depending on the results of subsequent immune evaluation
- rarely under specific antibody deficiency following re-emergence of severe significant infection requiring hospitalisation.

In principle, immunoglobulin therapy should only be continued or renewed if there is a demonstrated clinical benefit. Note that re-vaccination with unconjugated pneumococcal polysaccharide vaccine is not recommended because of the potential for immune hyporesponsiveness induced by repeated vaccination (O'Brien et al 2007).

On review of an authorisation period

Evidence of clinical effectiveness of Ig therapy, and criteria for continued use may include:

- A reduction in the frequency and severity of bacterial infections during the authorisation period.

AND

- A trial cessation of Ig for the purposes of immunological evaluation will be undertaken.

  OR

- A trial period of cessation of intravenous immunoglobulin (IVIg) for the purpose of immunological evaluation is medically contraindicated on safety grounds (such as a patient with neutropenia, on immunosuppressant medication or with clinically active bronchiectasis and/or suppurative lung disease).

Antibiotic therapy may be indicated in addition to immunoglobulin therapy.

Life-threatening infection or a series of serious infections following trial-off Ig therapy in patients with proven specific antibody deficiency.

Natural history of specific antibody deficiency remains poorly defined, although antibody production will improve for many patients over time, particularly children.

Regular review by a Clinical Immunologist is required, at least annually. Documentation of clinical effectiveness is necessary for continuation of Ig therapy.

Cessation of immunoglobulin therapy should be considered, at least after each 12 months of Ig therapy, extended as required to enable cessation of therapy in September or October.

This should particularly be considered in patients who do not have suppurative lung disease or bronchiectasis. An immunoglobulin washout period of four to six months is necessary to enable an accurate assessment. Prophylactic antibiotics may be considered to cover the period of cessation of immunoglobulin therapy.

Patients may qualify for further immunoglobulin therapy:

- under other immunodeficiency criteria (e.g. primary antibody deficiency disorder), depending on the results of subsequent immune evaluation
- rarely under specific antibody deficiency following re-emergence of severe significant infection requiring hospitalisation.

In principle, immunoglobulin therapy should only be continued or renewed if there is a demonstrated clinical benefit. Note that re-vaccination with unconjugated pneumococcal polysaccharide vaccine is not recommended because of the potential for immune hyporesponsiveness induced by repeated vaccination (O'Brien et al 2007).

On review of an authorisation period

Evidence of clinical effectiveness of Ig therapy, and criteria for continued use may include:

- A reduction in the frequency and severity of infections during the authorisation period.

AND

- A trial cessation of Ig for the purposes of immunological evaluation will be undertaken.

  OR

- A trial period of cessation of IVIg for the purpose of immunological evaluation is medically contraindicated on safety grounds (such as a patient with neutropenia, on immunosuppressant medication or with clinically active bronchiectasis and/or suppurative lung disease).

Antibiotic therapy may be indicated in addition to immunoglobulin therapy.

Patients currently receiving immunoglobulin therapy for a diagnosis of IgG subclass deficiency are eligible for continued therapy, but a diagnosis of specific antibody deficiency should be confirmed following cessation of immunoglobulin therapy.

Natural history of specific antibody deficiency remains poorly defined,

although antibody production will improve for many patients over time, particularly children.

Regular review by a Clinical Immunologist or Respiratory Physician is required, at least annually. Documentation of clinical effectiveness is necessary for continuation of Ig therapy.

Cessation of immunoglobulin therapy should be considered at least after each 12 months of Ig therapy, extended as required to enable cessation of therapy in September or October.

This should particularly be considered in patients who no longer have active bronchiectasis and/or suppurative lung disease. An immunoglobulin washout period of four to six months is necessary to enable an accurate assessment. Prophylactic antibiotics may be considered to cover the period of cessation of immunoglobulin therapy.

Patients may qualify for further immunoglobulin therapy:

- under other immunodeficiency criteria (e.g. primary antibody deficiency disorder), depending on the results of subsequent immune evaluation
- rarely under specific antibody deficiency following re-emergence of severe significant infection requiring hospitalisation.

In principle, immunoglobulin therapy should only be continued or renewed if there is a demonstrated clinical benefit. Note that re-vaccination with unconjugated pneumococcal polysaccharide vaccine is not recommended because of the potential for immune hyporesponsiveness induced by repeated vaccination (O'Brien et al 2007).

On review of an authorisation period

Evidence of clinical effectiveness of Ig therapy, and criteria for continued use may include:

- A reduction in the severity and frequency of infections during the review period.

  AND

- Clinically active bronchiectasis and/or suppurative lung disease persists.

AND

- A trial cessation of therapy will be undertaken next September or October to undertake an immunological re-evaluation.

  OR

- A trial period of cessation of intravenous immunoglobulin (IVIg) for the purpose of immunological evaluation is medically contraindicated on safety grounds (such as a patient with neutropenia, on immunosuppressant medication or with clinically active bronchiectasis and/or suppurative lung disease).

  AND

  A second physician has confirmed that cessation of IVIg for the purpose of immunological evaluation is medically contraindicated on safety grounds.

Antibiotic therapy may be indicated in addition to immunoglobulin therapy.

Dose	
	Prevention of infections in individuals with frequent infections who have demonstrated failure to mount protective IgG antibody responses to vaccine antigen challenge, despite normal total serum IgG levels. • **Maintenance Dose** - 0.4 g/kg every 4 weeks. **Loading dose:** not approved. Subcutaneous administration of immunoglobulin (SCIg) is a suitable alternative to IVIg in this setting. **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.**
	Life-threatening infection or a series of serious infections following trial-off Ig therapy in patients with proven specific antibody deficiency. • **Maintenance Dose** - 0.4 g/kg every 4 weeks. **Loading dose:** not approved. Subcutaneous administration of immunoglobulin (SCIg) is a suitable alternative to IVIg in this setting. **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.**
	Patients currently receiving immunoglobulin therapy for a diagnosis of IgG subclass deficiency are eligible for continued therapy, but a diagnosis of specific antibody deficiency should be confirmed following cessation of immunoglobulin therapy. • **Maintenance Dose** - 0.4 g/kg every 4 weeks. Subcutaneous administration of immunoglobulin (SCIg) is a suitable alternative to IVIg in this setting. **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.**

Bibliography

Bheng, YK, Decker, PA, O'Byrne, MM, et al 2006, 'Clinical and Laboratory characteristics of 75 patients with specific polysaccharide antibody deficiency syndrome', *Annals of Allergy, Asthma and Immunology*, vol. 97, no. 3, pp. 306–11.

Bonilla, FA, Bernstein, L, Khan, DA, et al 2005, 'Practice parameter for the diagnosis and management of primary immunodeficiency', *Annals of Allergy, Asthma and Immunology*, vol. 94, no. 5, suppl. 1, pp. S1–63.

O'Brien, KL, Hochman, M & Goldblatt, D 2007, 'Combined schedules of pneumococcal conjugate and polysaccharide vaccines: is hyporesponsiveness an issue?' *Lancet Infectious Diseases*, vol. 7, no. 9, pp. 597–606.

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.

Generated on: 31 March 2019