Secondary hypogammaglobulinaemia (including iatrogenic immunodeficiency)

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Condition for which IVIg has an emerging therapeutic role.

Specific Conditions	• Secondary hypogammaglobulinaemia (excluding haematological malignancies)
Indication for IVIg Use	• Replacement therapy for life-threatening infection due to hypogammaglobulinaemia related to other diseases, or medical therapy, including haemopoietic stem cell transplantation (HSCT) unrelated to haematological malignancy.
Level of Evidence	Nil (Category 4b)
Description and Diagnostic Criteria	Recurrent and/or severe bacterial infections may arise from hypogammaglobulinaemia of diverse causes. Hypogammaglobulinaemia may arise from protein-losing states, malnutrition and medical immunosuppression. In most cases, successful management of the underlying condition will reverse the immunodeficiency, restoring immunocompetence. In some cases, recurrent or severe infection may arise from secondary immunodeficiency where the underlying cause cannot be reversed, or where there are unwanted effects of removing or reducing immunosuppressive therapy. New immunosuppressive regimens, such as monoclonal B-cell depletion with Rituximab or similar agents, do not generally induce hypogammaglobulinaemia at standard doses. However, repeated cycles of B-cell depletion in combination with other agents used to treat life-threatening immune-mediated diseases may increase rates of infection related to hypogammaglobulinaemia.
Justification for Evidence Category	
Qualifying Criteria for IVIg Therapy	• Serum IgG less than the lower limit of the reference range tested on two separate occasions. AND • Underlying cause of hypogammaglobulinaemia cannot be reversed or measures to reverse are contraindicated. AND • At least one invasive or life-threatening bacterial infection in the previous 12 months. OR • Clinically active bronchiectasis confirmed by radiology. Antibiotic therapy may be indicated in addition to immunoglobulin therapy.
Exclusion Criteria	HIV in children. - see HIV in children Transplantation-related immunomodulation (kidney transplantation). - see Kidney transplantation

	Transplantation-related immunomodulation (solid organ transplantation other than kidney). - see Solid organ transplantation (other than kidney)
Review Criteria for Assessing the Effectiveness of IVIg Use	Initial review is required at six months by the Treating Medical Specialist and at least annually to assess the clinical benefit. Documentation of clinical effectiveness is necessary for continuation of Ig therapy. Cessation of Ig therapy should be considered at least after each 12 months of therapy, extended as required to enable cessation of therapy in September/October, with repeat clinical and/or immunological evaluation before re-commencement of therapy. **On review of an authorisation period** Clinical effectiveness of Ig therapy may be demonstrated by: • Adequate IgG levels and a reduction in the number and severity of any bacterial infections during the authorisation period. AND • A trial period of cessation of IVIg for the purpose of immunological evaluation is medically contraindicated on safety grounds (such as neutropenia, immunosuppressant medication, active bronchiectasis and/or suppurative lung disease or severe hypogammaglobulinaemia that persists where no significant improvement has occurred in the underlying condition). OR • A trial cessation of Ig for the purposes of immunological evaluation will be undertaken. In principle, IVIg should be continued or renewed only if there is a demonstrated clinical benefit. Antibiotic therapy may be indicated in addition to immunoglobulin therapy.

Dose	
	• **Loading Dose** - one additional dose of 0.4 g/kg in the first month of therapy is permitted if the serum IgG level is <4 g/L. • **Maintenance in chronic suppurative lung disease** - dosing to achieve IgG trough level of up to 9 g/L is permitted if chronic suppurative lung disease is not adequately controlled at an IgG trough level at the lower limit of the age-specific serum IgG reference range, at a total dose of 1 g/kg per month. • **Maintenance Dose** - 0.4 g/kg every four weeks, or more frequently, to achieve IgG trough level of at least the lower limit of the age-specific serum IgG reference range. Subcutaneous administration of immunoglobulins is a suitable alternative to IVIg in this condition, a suggested dose is 0.1 g/kg lean body mass every week, modified to achieve a serum IgG level of at least the lower limit of the age-specific serum IgG reference range. **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

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.

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