



Summary of Key Changes to the *Criteria for the clinical use of intravenous immunoglobulin in Australia Second Edition*

Indications that have been removed from the IVIg Criteria

Chapter	Indication	Change
6	Haemopoietic stem cell transplantation (HSCT) for prevention of GvHD in high risk Allogeneic HSCT	<p>The removal of the indication is based on the latest published clinical literature, which concludes that the routine prophylactic treatment of HSCT with IVIg is not supported in the absence of hypogammaglobulinaemia.</p> <p>Patients with hypogammaglobulinaemia may still be eligible to receive IVIg under the acquired hypogammaglobulinaemia indication.</p> <p>Page 148, 2007 Criteria</p>
7	Sepsis - neonatal	<p>IVIg is no longer funded for the treatment of sepsis in neonates. The 2011 International Neonatal Immunotherapy Study¹ found that therapy with IVIg had no effect on the outcomes of suspected or proven neonatal sepsis.</p> <p>Page 193, 2007 Criteria.</p>

New Indications

Chapter	Indication	Change
7	Hashimoto encephalopathy	<p>New indication. 'Hashimoto encephalopathy (steroid-responsive encephalopathy associated with autoimmune thyroiditis). IVIg is not supported as first-line treatment, because preferable alternative treatments are available. IVIg may be considered in exceptional circumstances where there is progressive neurologic decline despite appropriate steroid therapy.'</p> <p>Page 197, IVIg Criteria Second Edition.</p>
7	Limbic encephalitis - nonparaneoplastic	<p>New indication. 'Limbic encephalitis - nonparaneoplastic. There appears to be a role for IVIg in nonparaneoplastic limbic encephalitis associated with neuronal antibodies to cell surface antigens. This includes VGKC antibodies, as well as NMDA receptor antibodies and AMPA receptor antibodies.'</p> <p>Page 198, IVIg Criteria Second Edition.</p>

¹ Brockelhurst et al. International Neonatal Immunotherapy Study (INIS) Collaborative Group. Treatment of Neonatal Sepsis with Intravenous Immune Globulin. *N Engl J Med* 2011;365: 1201-11

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7	Pyoderma gangrenosum	New indication. 'Pyoderma gangrenosum. Use of IVIg is limited to patients with significant pyoderma gangrenosum, diagnosed by a dermatologist, unresponsive to corticosteroids and other immunosuppressive agents. Induction dose, then maintenance therapy up to 6 months. Should be ceased in patients who fail to respond after 3 cycles.' Page 205, IVIg Criteria Second Edition.
7	Rasmussen Syndrome	It was previously listed under 'Epilepsy - rare childhood cases', and only available to children. It is now available to adults too; however, the prevalence in adults is extremely rare. Page 206, IVIg Criteria Second Edition.
7	Systemic Capillary Leak Syndrome	New indication. 'Systemic capillary leak syndrome (SCLS). SCLS is an extremely rare condition that is characterised by life-threatening attacks of reversible capillary hyperpermeability accompanied by haemoconcentration and hypoalbuminaemia. A diagnosis by a consultant physician, emergency specialist, or intensive care unit specialist is required.' Approval will be provided for an initial period of 12 months only. Ongoing therapy will require the clinician to confirm in writing that the patient experienced a reduced number of severe episodes when treated with IVIg. Page 210, IVIg Criteria Second Edition.
8 Not supported	Behcet's disease	Behcet's disease is a rare immune-mediated systemic vasculitis that often presents with mucous membrane ulceration and ocular involvements. It can also involve the gastrointestinal tract, lungs, CNS, and joints. IVIg is not supported. Page 215, 2012 IVIg Criteria Second Edition.
8 Not supported	Lupus cerebritis	'IVIg is not supported as preferable alternative treatments are available.' Page 215, IVIg Criteria Second Edition.

Changes to indications to clarify review criteria for continuation of IVIg therapy

Chapter	Indication	Change
5	Acquired hypogammaglobulinaemia secondary to haematological malignancies	<p>The key change to the acquired hypogammaglobulinaemia secondary to haematological malignancies indication is that the treating clinician is required to review the patient every 6 months and consider stopping treatment at 12 months to re-evaluate the patient's immune system.</p> <p>Cessation of IVIG after each 12 months still requested but now based on clinical circumstance and system for collecting data clarified. Ongoing therapy will require confirmation in writing from treating physician that:</p> <ul style="list-style-type: none"> i) an annual review has taken place; ii) there is demonstrable clinical benefit; and iii) trial cessation is '<i>medically contraindicated on safety grounds</i>'. <p>Exclusion criteria have also been added to the indication i.e. HIV in children, transplantation-related immunomodulation, secondary hypogammaglobulinaemia.</p> <p>Page 48, IVIg Criteria Second Edition.</p>
5	Inflammatory myopathies	<p>Regular review may now be undertaken by one of three types of physicians, a neurologist, rheumatologist or clinical immunologist (compared with the previous 'neurologist' only). This is now in line with the qualifying criteria.</p> <p>Page 73, IVIg Criteria Second Edition.</p>
6	Secondary hypogammaglobulinaemia (including iatrogenic immunodeficiency)	<p>The frequency of review has increased from annually to 6 monthly. Cessation at 12 months still requested but it is now based on clinical circumstances. Regular review can be now be performed by '<i>the treating physician</i>' (compared with previous requirement for an immunologist). Ongoing therapy after each 12 month period will require confirmation in writing from treating physician that:</p> <ul style="list-style-type: none"> i) an annual review has taken place; ii) there is demonstrable clinical benefit; and iii) trial cessation is '<i>medically contraindicated on safety grounds</i>'. <p>Page106, IVIg Criteria Second Edition.</p>

Chapter	Indication	Change
6	Specific antibody deficiency (including IgG subclasses)	<p>1. Specific antibody deficiency: the requirements to cease and review have been strengthened. Ongoing therapy after each 12 month period will require confirmation in writing from clinical immunologist that:</p> <ul style="list-style-type: none"> i) an annual review has taken place; ii) there is demonstrable clinical benefit; and iii) trial cessation is 'medically contraindicated on safety grounds'. <p>2. IgG subclass deficiency: this is not an approved indication for new patients. Existing patients will now require either a confirmed IgG deficiency (and thus be eligible under another indication) or clinically active bronchiectasis/suppurative lung disease. In the latter case, ongoing therapy (after each 12 month period) will require confirmation in writing by a clinical immunologist that:</p> <ul style="list-style-type: none"> i) an annual review has taken place; ii) there is demonstrable clinical benefit; and iii) trial cessation is 'medically contraindicated on safety grounds', and confirmation in writing by a second physician that a <i>'trial cessation is medically contraindicated on safety grounds'</i>. <p>Page 110, IVIg Criteria Second Edition.</p>

*** Please note that, apart from Primary Immunodeficiency Diseases, all other indications for IVIg for immune replacement will now require confirmation **in writing** from one or more physicians for ongoing therapy***

Minor wording changes to clarify indications

Chapter	Indication	Change
5	Idiopathic (autoimmune) thrombocytopenia purpura (ITP) in adults	<p>There have been several minor changes to the wording. Indications for use now include the following additional clarification:</p> <ul style="list-style-type: none"> 1. Refractory acute ITP '<i>on the recommendation of a clinical haematologist</i>'; 4. Specific circumstances '<i>b. other concurrent risk factors for bleeding (e.g. concurrent anti-coagulant therapy)</i>'; and d. Chronic ITP '<i>under the guidance of a clinical haematologist, as adjunctive therapy or where other therapies have failed or are not appropriate</i>'. <p>Page 66, IVIg Criteria Second Edition.</p>
5	Multifocal motor neuropathy	<p>The presence of persistent conduction block is now no longer necessary to qualify for IVIg therapy. The exclusion criteria now include '<i>significant sensory impairment without an adequate alternative explanation</i>'.</p> <p>Page 87, IVIg Criteria Second Edition.</p>
7	Epilepsy – rare childhood cases	<p>Rasmussen syndrome has been listed separately from the 'epilepsy' listing.</p> <p>The epilepsy indication has been strengthened by including a requirement for a full assessment by a paediatric neurologist.</p> <p>Page 194, IVIg Criteria Second Edition.</p>

Chapter	Indication	Change
7	Potassium channel antibody-associated encephalopathy	Minor wording changes have been made to specify syndrome names. Page 202, IVIg Criteria Second Edition.
7	Diabetic amyotrophy	This condition has been renamed (previously listed as ' <i>autoimmune diabetic neuropathy</i> '). The indication has been more explicitly defined. Explicitly requires failure or intolerance of steroids. Page 194, IVIg Criteria Second Edition.
7	Paraneoplastic syndromes	The paraneoplastic syndromes are now more explicitly defined and are listed separately under three separate indications: Paraneoplastic cerebellar degeneration, Limbic encephalitis (paraneoplastic) and Paraneoplastic subacute sensory neuropathy. Page 200, IVIg Criteria Second Edition
7	Catastrophic antiphospholipid syndrome	Minor wording changes were made to clearly specify the qualifying criteria and dose. Pg 189, IVIg Criteria Second Edition
7	Myocarditis in children	The changes to the myocarditis in children indication stems from the November 2008 clarification process, which removed the requirement to conduct an invasive test that does not provide results in a timely way and has the potential to cause harm. Page 198, IVIg Criteria Second Edition