

2017 (v3.0) Proposed changes to version 2.1 of the Criteria for the clinical use of intravenous immunoglobulin in Australia

CONDITION NAME IN v2.1	Diabetic amyotrophy (diabetic proximal neuropathy or diabetic lumbosacral radiculoplexus neuropathy)
<p>PROPOSED APPROACH:</p> <p>To move Diabetic amyotrophy or diabetic lumbosacral radiculoplexus neuropathy (DLRPN) from <i>Exceptional circumstances only to Not supported.</i></p>	<p>SUMMARY OF RATIONALE:</p> <p>The recommendation is supported by factors including that:</p> <ul style="list-style-type: none"> • Improvement in symptoms usually occurs slowly but spontaneously in almost all patients, although recovery may be incomplete. • The recommendation to no longer support this condition is consistent with recommendations of the Canadian (Ontario Regional Blood Coordinating Network, 2016) and North American (National Guideline Clearinghouse, 2012) IVIg criteria. It is listed in the UK Guidelines (UK Department of Health, 2011) as a ‘grey’ condition under ‘Presumed immune-mediated disorders with little or no evidence of efficacy. • There are no published controlled clinical trials of the use of IVIg in DLRPN. One registered randomized clinical trial was terminated prematurely without publication (NCT00004407) and no abstract was published. • Case series have provided conflicting results in regard to response of neuropathic pain, but none have documented improvement in muscle weakness, atrophy or neurologic disability. One case series described 3 patients who had severe and progressive DLRPN despite active immunosuppressive therapy including IVIg. • A single prospective, randomized double-blind controlled trial of intravenous methylprednisolone, demonstrated significantly more improvement in neuropathic pain in the IVMP group, but no significant improvement in neuropathy impairment score (Class 1). • Ig use in Australia is very low with between zero and fifteen patients receiving treatment annually for the last five years.
<p>Role of Ig therapy: Diabetic amyotrophy, also referred to as diabetic lumbosacral radiculoplexus neuropathy, is a multifocal, asymmetric, painful, acute or subacute neuropathic disorder affecting multiple levels of lumbosacral plexus, nerve roots, and distal nerves that emerge from the plexus. The clinical picture is that of unilateral or asymmetric bilateral pain, weakness and wasting in the lower limbs, usually associated with significant weight loss. Most cases occur while diabetes is under good control. LRPN can occur in nondiabetic patients. Whilst predominantly a motor syndrome, sensory and autonomic involvement can occur. The pathophysiology is thought to be immune-mediated and characterized by ischemic damage, inflammation and micro-vasculitis. Improvement in symptoms occurs in almost all patients spontaneously although recovery is delayed and may be incomplete.</p>	

Access Information in v2.1	
Condition Category	Condition for which Ig use is in exceptional circumstances only (Chapter 7)
Level of Evidence	Insufficient data (Category 4a)
Description	(Blank)
Qualifying Criteria	Intravenous immunoglobulin (IVIg) may be considered in exceptional circumstances for intractable pain or progressive muscle weakness in patients in whom steroids are ineffective or cannot be tolerated. This condition is monophasic and usually self-limiting. A single treatment may be sufficient, although monthly infusions for up to six months may be required for recurrent pain.
References (most recent update: May 2016)	
<p>Tamburin S, Magrinelli F, Favaro F, Briani C and Zanette G (2013) Long-term response of neuropathic pain to intravenous Immunoglobulin in Relapsing Diabetic Lumbrosacral Radiculoplexus Neuropathy. A Case report. <i>Pain Practice</i>, 14:85-90. http://onlinelibrary.wiley.com/doi/10.1111/papr.12133/full</p> <p>Pascoe MK, Low PA, Windebank AJ and Litchy WJ (1997) Subacute Diabetic Proximal Neuropathy. <i>Mayo Clinic Proceedings</i>, 72:1123-1132. http://www.sciencedirect.com/science/article/pii/S0025619611636744</p> <p>Thaisetthawatkul P and Dyck PJB (2010) Treatment of Diabetic and nondiabetic Lumbosacral Radiculoplexus neuropathy. <i>Current treatment options in Neurology</i>, 12:95-99. http://link.springer.com/article/10.1007/s11940-010-0059-8</p> <p>Ontario Regional Blood Coordinating Network (2016). Ontario Intravenous Immune Globulin (IVIg) Utilization Management Guidelines, Version 3.0. [online]. Available at: http://transfusionontario.org/en/download/ontario-intravenous-immune-globulin-IVIg-utilization-management-guidelines-2/.</p> <p>National Guideline Clearinghouse (NGC) (2012) Guideline summary: Evidence-based guideline: intravenous immunoglobulin in the treatment of neuromuscular disorders. Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. In: National Guideline Clearinghouse (NGC) [online]. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ). Available at: https://www.guideline.gov</p> <p>Zochodne DW, Isaac D and Jones C (2003) Failure of immunotherapy to prevent, arrest or reverse diabetic lumbosacral plexopathy. <i>Acta Neurologica</i></p>	

Scandinavica, 107:299-301.

<http://onlinelibrary.wiley.com/doi/10.1034/j.1600-0404.2003.02107.x/full>

Tamburin S. and Zanette Giampietro Z (2009) Intravenous Immunoglobulin for the treatment of diabetic lumbosacral radiculoplexus neuropathy . *Pain Medicine*, 10(8):1476-1480.

<https://academic.oup.com/painmedicine/article/15/9/1640/1894529/Diagnostic-and-Therapeutic-Pitfalls-in-Considering>

POTENTIAL OPERATIONAL IMPACT						
<p>Given that this condition will no longer be supported, any patients on ongoing therapy will need to be transitioned from Ig therapy to alternative treatments (see below). Following public consultation and the subsequent endorsement by governments, specific communication with relevant prescribers (and patients) would occur to support doctors caring for any patients on ongoing Ig therapy at that time. It is anticipated that the timing of any existing patient transition would be concurrent with implementation of BloodSTAR v3.0. Advice to prescribers will precede this date so that patients can transition to alternative medication or a different treatment approach, as appropriate.</p>						
POTENTIAL IMPACT ON PATIENTS, DEMAND AND EXPENDITURE						
Description of impact on patients:		<p>The best clinical results in the treatment of Diabetic amyotrophy have been demonstrated in patients treated with steroid therapy. It is recognised that almost all patients with this condition will slowly improve irrespective of the treatment given, although recovery may be delayed and may be incomplete in some patients. No treatment (including Ig therapy) has been shown to reduce the degree of muscle weakness, wasting or neurologic disability experienced by patients. For these reasons access to Ig therapy is recommended to no longer be supported. It is inappropriate to treat patients with medication that has no demonstrable benefit and in addition, there are small but not insignificant risks of harm from Ig therapy, as well as a high cost.</p> <p>Ig treatment for this condition is usually only for short term use, so very few patients are likely to be on treatment at the time of transition to the new criteria. However, it is anticipated that prescribers (and thus patients) would be informed of any decision once governments have endorsed this recommendation so that ample lead time is provided for prescribers to manage and transition patients to an alternative treatment approach if required. Importantly, there are effective new medications to treat neuropathic pain that are now available on the PBS and these agents are likely to be more effective for pain control than Ig therapy.</p>				
Impact on demand:		<p>The reallocation of Diabetic amyotrophy to <i>Not supported</i> means that immediate demand for Ig therapy for this condition would reduce in line with the number of patients being treated at the time of implementation. The annual demand impact is estimated to be a reduction of up to 4,000 g.</p>				
	2011-12	2012-13	2013-14	2014-15	2015-16	Estimated number of patients that will be affected – up to 15. The Specialist Working Group estimated magnitude of effect: Marginal: <\$500K reduction against projected demand
Patient number	0	10	6	15	9	
Total Grams issued	0	2,427	1,800	3,726	2,912	

% Total Grams issued	0.00%	0.07%	0.04%	0.08%	0.06%	
Specialist Working Group knowledge development opportunities and recommendations relevant to the transition to v3.0						
None identified at this stage.						

END OF PUBLIC CONSULTATION DOCUMENT
Next review: Two years after BloodSTAR v3.0 implemented