

2017 (v3.0) Proposed changes to v2.1 of the Criteria for the clinical use of intravenous immunoglobulin in Australia

<p>CONDITION NAME IN v2.1</p>	<p>Paraneoplastic neurological syndromes</p> <ul style="list-style-type: none"> - Paraneoplastic subacute sensory neuropathy - Paraneoplastic cerebellar degeneration
<p>PROPOSED APPROACH:</p> <p>To move paraneoplastic neurological syndromes from <i>Exceptional circumstances only to Not supported</i></p> <p>Note: The clinical conditions included in this category are:</p> <ul style="list-style-type: none"> • Paraneoplastic subacute sensory neuropathy (anti-Hu, Ri, CV2/CRMP5 in 80% patients) • Paraneoplastic cerebellar degeneration (anti-Yo, Ma2, Hu, Ri in 60% patients) 	<p>SUMMARY OF RATIONALE:</p> <p>The recommendation is supported by factors including that:</p> <ul style="list-style-type: none"> • These specific paraneoplastic neurologic syndromes are usually associated with onconeural antibodies directed against intracellular antigens (Hu, Ri, Ma2, CV2/CRMP5, Yo). Response to immune therapy is poor in these disorders, likely due to cytotoxic T-cell mediated neuronal loss. • Therefore, onconeural autoantibodies are considered biomarkers for the presence of tumours rather than pathogenic mediators of neurologic disease, and should motivate the search for an associated malignancy. • Tumour resection and/or oncological treatment remain the most effective therapies for these paraneoplastic neurologic syndromes, with case series reporting variable roles for corticosteroids, cyclophosphamide and rituximab. Ig use has been steadily increasing from 2012-13 to 2014-15 and this Ig use is not cost effective. • ‘Paraneoplastic disorders that are known not to be B- or T- cell mediated’ is included under ‘Presumed immune-mediated disorders with little or no evidence of efficacy’ as a ‘grey’ condition in the NHS Clinical Guidelines for Ig Use (UK Department of Health, 2011) and the condition is not listed in the Canadian Guidelines IVIg Management Guidelines (Ontario Regional Blood Coordinating Network, 2016).
<p>Role of Ig therapy, if appropriate: Not applicable</p>	
<p>Access Information in v2.1 as at October 2016</p>	

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	<p>Paraneoplastic subacute sensory neuropathy</p> <p>Intravenous immunoglobulin (IVIg) may be indicated in select cases, in combination with tumour therapy (tumour resection and/or oncological treatment), where the latter has not led to an improvement in the neurologic syndrome; where other immunomodulatory therapies are contraindicated or have failed; or if the neurologic features warrant urgent intervention.</p> <p>Paraneoplastic cerebellar degeneration</p> <p>IVIg may be indicated in select cases, in combination with tumour therapy (tumour resection and/or oncological treatment), where the latter has not led to an improvement in the neurologic syndrome; where other immunomodulatory therapies are contraindicated or have failed; or if the neurologic features warrant urgent intervention.</p> <p>Note: that Limbic encephalitis – paraneoplastic is considered separately.</p>
References	
<p>Bataller L, Galiano R, Garcia-Escrig M, Martinez,B, Sevilla T, Blasco R, et al (2010) Reversible paraneoplastic limbic encephalitis associated with antibodies to the AMPA receptor. <i>Neurology</i>, 74(3):265–7.</p> <p>https://www.ncbi.nlm.nih.gov/pubmed/20083804</p> <p>Henry C, Husson H, de Broucker T (2009). Autoimmune limbic encephalitis with anti-NMDA receptor antibodies and ovarian teratoma: a treatable form of paraneoplastic limbic encephalitis’ (in French), <i>Revue neurologique (Société de neurologie de Paris)</i>, 165(1):70–5.</p> <p>https://www.ncbi.nlm.nih.gov/pubmed/18809188</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-ivi-g-utilization-management-guidelines-2/.</p> <p>UK Department of Health (2011) Clinical Guidelines for Immunoglobulin Use: Second Edition Update. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216671/dh_131107.pdf</p>	

UK Department of Health (2011) Clinical Guidelines for Immunoglobulin Use: Second Edition Update: Summary Poster. Available at: https://www.igd.nhs.uk/wp-content/uploads/2016/04/DemandManagementPoster_v4_February2016.pdf

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 (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 at the time of 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						
<p>Description of impact on patients:</p>		<p>The symptoms of Paraneoplastic Subacute Sensory Neuropathy or Paraneoplastic cerebellar degeneration are caused by antibodies made by a tumour. The best clinical results for these conditions are therefore demonstrated after the tumour has been removed or treated with chemotherapy. In fact, more recent publications have failed to demonstrate any benefit in response to Ig therapy because the antibodies causing the symptoms are directed at proteins inside brain cells and the Ig is therefore ineffective. There are also alternative medications (including steroids and other therapies) that can be used to more effectively to address the symptoms while waiting for tumour resection and/or the chemotherapy to take effect.</p> <p>In addition, it is inappropriate to treat patients with medication that has no demonstrable benefit and there are small but not insignificant risks of harm from Ig therapy, as well as a high cost.</p> <p>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 any existing patients to an alternative treatment approach, if required at that time.</p>				
<p>Impact on demand:</p>		<p>Demand for Ig therapy under these conditions has been steadily increasing over the last 3 years. Given the recognition that Ig therapy is ineffective for immunomodulation of autoantibodies to intracellular neural antigens, it is likely that the treatment has been ineffective. The reallocation of these two paraneoplastic syndromes to <i>Not supported</i> means that immediate demand for Ig therapy for these conditions would reduce in line with the number of patients being treated at the time of implementation.</p>				
	2011-12	2012-13	2013-14	2014-15	2015-16	<p>The Specialist Working Group estimated magnitude of effect: Marginal: <\$500K reduction against projected</p>
Patient number	0	15	12	21	27	

PUBLIC CONSULTATION 2017 –Paraneoplastic syndromes (Paraneoplastic subacute sensory neuropathy and Paraneoplastic cerebellar degeneration)

Total Grams issued	0	2,834	2,969	5,254	6,183	demand
% Total Grams issued	0.00%	0.08%	0.07%	0.12%	0.12%	

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.