

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

CONDITION NAME IN v2.1	Pure white cell aplasia (PWCA)
<p><b>PROPOSED APPROACH:</b></p> <p>To move Pure white cell aplasia from <i>Exceptional circumstances only to Not supported with the changes as outlined.</i></p>	<p><b>SUMMARY OF RATIONALE:</b></p> <p>The recommendation is supported by factors including that:</p> <ul style="list-style-type: none"> <li>• There have been no published randomised clinical trials in PWCA and the only published evidence remains to be single case presentations (Barbui et al, 1984 and Kim et al, 2016) reporting vague associations of response to IVIg.</li> <li>• Spontaneous resolution is expected following the removal of causal agents and treatment of underlying conditions with G-CSF (Granulocyte - Colony Stimulating Factor).</li> <li>• Alternate therapies of G-CSF, steroids, or other immunosuppressive treatments exist for this disorder.</li> <li>• IVIg is not recommended for PWCA in the Canadian (Ontario Regional Blood Coordinating Network, 2016) or UK guidelines (UK Department of Health, 2011) for IVIg use.</li> <li>• There has been negligible Ig use for this condition over the last 5 years (zero in the past two years).</li> </ul>
<p><b>Role of Ig therapy, if appropriate:</b> PWCA is very uncommon with patients presenting clinically with severe neutropenia, recurrent infections and profound agranulocytosis on bone marrow biopsy. The condition has been associated with autoimmune diseases, drug induced or viral exposures. Treatment varies but is centred on immunosuppression with the removal of any offending agents and treatment with G-CSF. While some reported cases have been treated with Ig therapy in combination with the above, alternative therapies are seen to be more effective and the evidence of any additional benefit from Ig therapy is very weak. PWCA is not listed in international Guidelines for IVIg utilization in Canada (Ontario Regional Blood Coordinating Network, 2016) or the United Kingdom (UK Department of Health, 2011).</p> <p>Where neutropenia is related to an underlying autoimmune process, that condition (Autoimmune neutropenia) has been retained.</p>	
Access Information in v2.1	
<b>Condition Category</b>	Condition for which Ig use is in exceptional circumstances only (Chapter 7)
<b>Level of Evidence</b>	No included studies (Category 4b)
<b>Description</b>	PWCA is a rare syndrome of severe neutropenia and a selective deficiency of granulocyte progenitors. Intravenous immunoglobulin (IVIg) is a reasonable option for patients with immunological PWCA who have

	failed other therapies (e.g. prednisone or cyclosporine).
<b>Qualifying Criteria</b>	<b>Blank</b>
<b>References</b> <b>(most recent update: March 2016)</b>	
<p>Barbui T, Bassan R, Viero P, Minetti B, Comotti B and Buelli M (1984) Pure white cell aplasia treated by high dose intravenous immunoglobulin. <i>British Journal of Haematology</i>, 58(3):554-555.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/6498105">https://www.ncbi.nlm.nih.gov/pubmed/6498105</a></p> <p>Kim PG, Suh J, Adelman M, Oduro K, Williams E, Brunner A and Kuter D (2016) Pure white cell aplasia and Necrotizing Myopathies. <i>Case Reports in Hematology</i>, 2016, Article ID 4161679, 5 pages.</p> <p><a href="https://www.hindawi.com/journals/crihem/2016/4161679/">https://www.hindawi.com/journals/crihem/2016/4161679/</a></p> <p>Ontario Regional Blood Coordinating Network (2016). Ontario Intravenous Immune Globulin (IVIg) Utilization Management Guidelines, Version 3.0. [online]. Available at: <a href="http://transfusionontario.org/en/download/ontario-intravenous-immune-globulin-ivi-utilization-management-guidelines-2/">http://transfusionontario.org/en/download/ontario-intravenous-immune-globulin-ivi-utilization-management-guidelines-2/</a>.</p> <p>UK Department of Health (2011) Clinical Guidelines for Immunoglobulin Use: Second Edition Update. Available at: <a href="https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216671/dh_131107.pdf">https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216671/dh_131107.pdf</a></p> <p>UK Department of Health (2011) Clinical Guidelines for Immunoglobulin Use: Second Edition Update: Summary Poster. Available at: <a href="https://www.igd.nhs.uk/wp-content/uploads/2016/04/DemandManagementPoster_v4_February2016.pdf">https://www.igd.nhs.uk/wp-content/uploads/2016/04/DemandManagementPoster_v4_February2016.pdf</a></p>	

<b>POTENTIAL OPERATIONAL IMPACT</b>						
<p>Given the absence of use over recent years, there is not anticipated to be any significant operational impact arising from the proposed changes. Following public consultation and the subsequent endorsement by governments, specific communication with any current prescribers / patients would occur. It is anticipated that the timing of existing patient transition would be at the time of implementation of v3.0. Advice to prescribers would precede this date so that Ig therapy weaning of any existing patients can occur, if required.</p>						
<b>POTENTIAL IMPACT ON PATIENTS, DEMAND AND EXPENDITURE</b>						
<b>Description of impact on patients:</b>		<p>It is recognised that this condition is very rare and alternative therapies have been demonstrated to be more effective in treatment than Ig therapy. These therapies are available and are being used in Australia, and therefore access to Ig therapy will no longer be supported. Given the very low level of use over the last few years for this condition, it is clear that where patients have received Ig therapy, it has been for very short periods of treatment only. It is therefore unlikely that there would be any impact to ongoing patient care at the time of transition. It is recognised that that for any patients with Autoimmune neutropenia, which is a condition with very low white cell counts, Ig therapy will continue to be supported. It is possible that the patients treated under this condition, did in fact have Autoimmune neutropenia.</p>				
<b>Impact on demand:</b>		<p>There has been minimal use for this condition over the last 5 years and thus the withdrawal of access is anticipated to be minimal with no material impact on demand.</p>				
	<b>2011-12</b>	<b>2012-13</b>	<b>2013-14</b>	<b>2014-15</b>	<b>2015-16</b>	<p>Estimated number of patients that will be affected.  The Specialist Working Group estimated magnitude of effect:  No impact against projected demand</p>
<b>Patient number</b>	<5	0	<5	0	0	
<b>Total Grams issued</b>	<500	0	<500	0	0	
<b>% Total Grams issued</b>	<0.02%	0.000%	<0.01%	0.000%	0.00%	
<b>Specialist Working Group knowledge development opportunities and recommendations</b>						
<p>None identified at this stage.</p>						

**END OF PUBLIC CONSULTATION DOCUMENT**

**Next review: Two years after BloodSTAR v3.0 implemented**