

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

v2.1 CONDITION NAME: Autoimmune uveitis	
v3.0 CONDITION NAME: Autoimmune retinopathy (AIR)	
PROPOSED APPROACH: To retain Autoimmune retinopathy in <i>Exceptional circumstances only</i> with changes as outlined.	SUMMARY OF RATIONALE: <p>The recommended changes are supported by factors including that:</p> <ul style="list-style-type: none"> - Although not commonly prescribed, Ig therapy should remain as an option for use for patients with persistent severe Autoimmune Retinopathy (AIR) and anti-retinal antibodies as it is a rare condition associated with severe, progressive and irreversible visual loss. - The need for ongoing access to Ig therapy has been confirmed by, and these criteria have been developed in consultation with, the Royal Australian and New Zealand College of Ophthalmologists' (RANZCO) Therapeutics Committee and the RANZCO Uveitis Special Interest Group. - The criteria have been developed to place Ig therapy as third line treatment (or second line if Rituximab is unavailable) in patients with refractory persistent and severe disease, and specific diagnostic requirements have been defined. - The use of Ig therapy is very low with less than five patients being treated annually for the last 5 years. - This very rare indication is listed in the Clinical Guidelines for Ig Use of the United Kingdom (UK Department of Health, 2011) - when eyesight is threatened - but not the Canadian IVIg Utilisation Management Guidelines (Ontario Regional Blood Coordinating Network, 2016), but may be approved for funding at the local level.
v2.1 CONDITION CATEGORY: Condition for which Ig is used in exceptional circumstances only (Chapter 7) v3.0 CONDITION CATEGORY: Condition for which Ig is used in exceptional circumstances only (Chapter 7)	

Role of Ig therapy: : Ig therapy should be considered for patients with Autoimmune retinopathy as a treatment of “last resort” for refractory severe disease because of the severe, progressive and irreversible nature of the visual loss in these patients, and the demonstrated autoimmune nature of the disease (as evidenced by the presence of anti-retinal antibodies). Use in Australia is very low which is in line with expected prevalence of refractory disease as patients will usually respond to alternative therapies.

First line treatment of AIR is with at least three months of corticosteroid therapy and at least two immunosuppressant medications (such as cyclosporine, methotrexate and rituximab). Although Rituximab (anti-B cell monoclonal Ab) has been used to treat AIR, it has been used with mixed success, and it is noted that access to Rituximab in Australia remains limited.

For refractory patients responding to Ig therapy, the value lies in arresting decline rather than necessarily causing an improvement in function. Long term use of intravenous immunoglobulin may be required in cases where cessation of treatment is accompanied by disease progression.

ITEM	CRITERIA v2.1	PROPOSED REVISIONS TO THE CRITERIA	SPECIALIST WORKING GROUP RATIONALE FOR ADDITIONS/CLARIFICATIONS
Condition Name	Autoimmune uveitis	Autoimmune retinopathy	Name change was recommended by the College of Ophthalmology and better describes the eligible sub-group of patients with Autoimmune uveitis.
Specialty	Immunology	Immunology	No change
Category	<i>Exceptional use only</i>	<i>Exceptional use only</i>	No change
Specific Conditions	Autoimmune uveitis	Autoimmune retinopathy (AIR)	Name change reflected in specific conditions
Level of Evidence	Insufficient data (Category 4a)	Insufficient data (Category 4a)	No change
Justification for Evidence Category		While there is little high level evidence conclusively demonstrating benefit of Ig therapy, AIR is a very rare condition and open label studies and case series do demonstrate some benefit including recent publications	Justification for Evidence drafted based on consultation of the literature and advice from the Royal Australian and New Zealand College of Ophthalmologists (RANZCO).

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		(Castiblanco & Foster, 2014 and Garcia-Geremias, 2015). It is important to acknowledge that autoimmune retinopathy is sight threatening and when refractory to corticosteroid and immunosuppressant therapy, observational studies conclude that Ig therapy is well-tolerated and effective in arresting disease in some patients.	
Indications		Autoimmune Retinopathy that is sight threatening and refractory to corticosteroid and immunosuppressant therapy	
Description and Diagnostic Criteria	Uveitis refers to inflammation of the uvea of the eye and can be caused by infection, exposure to toxins or autoimmune disorders. Symptoms may include redness of the eye, blurred vision, unusual sensitivity to light, dark floating spots in the vision and eye pain. Ocular inflammation of this kind may threaten sight and be resistant to standard	<p>Autoimmune retinopathy (AIR) is the main disease within the broader condition of ‘uveitis’. AIR can be associated with severe, progressive and irreversible visual loss and demonstration of anti-retinal antibodies. Symptoms may include, blurred vision, dark floating spots in the vision field and sub-acute visual loss. Ig therapy may be used to treat autoimmune sight-threatening retinopathy that is refractory to both corticosteroid and immunosuppressant therapy. Although Rituximab has been used to treat AIR, it has had mixed success, and its access in Australia remains limited.</p> <p>The value of treatment may lie in arresting decline rather than causing an improvement in function. Indicators of disease status include visual acuity, visual field, electroretinography and integrity of macular anatomy by optical coherence tomography testing.</p>	<p>The description and diagnostic criteria were substantially revised following consultation of the literature and advice from RANZCO.</p> <p>The focus for Ig therapy has been narrowed to autoimmune sight-threatening retinopathy refractory to both corticosteroid and immunosuppressant therapy.</p> <p>The treatment goal now includes arresting decline rather than functional improvement alone.</p>

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	immunosuppression. Intravenous immunoglobulin (IVIg) therapy may be considered for immune-mediated, sight- threatening uveitis with persistent activity despite both oral corticosteroid and systemic immunosuppressive therapy. Uveitis of non-immune origin is not indicated.				
Diagnosis is required		Yes	By which specialty	Any specialist	Must now be diagnosed by a specialist noting that the qualifying criteria require the diagnosis to be either made or confirmed by an ophthalmologist .
Diagnosis must be verified		No	By which specialty		
Exclusion Criteria	Uveitis of non-immune origin is not indicated.	Uveitis with features of anterior or posterior chamber inflammation.			The exclusion criteria describe types of uveitis which are not eligible for Ig therapy.
Qualifying		<ul style="list-style-type: none"> Diagnosis made or confirmed by an ophthalmologist 			Qualifying criteria drafted following consultation with

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Criteria		<p>AND</p> <ul style="list-style-type: none"> Persistent severe disease threatening eyesight limited to the retinal plane confirmed by ERG with integrity of macular anatomy confirmed by optical coherence tomography testing <p>AND</p> <ul style="list-style-type: none"> Poorly responsive to oral or intravenous corticosteroid therapy for at least three months <p>OR</p> <ul style="list-style-type: none"> Corticosteroid therapy is contraindicated or has resulted in unacceptable side effects or significant toxicity <p>AND</p> <ul style="list-style-type: none"> Unresponsive to at least two immunosuppressant agents <p>OR</p> <ul style="list-style-type: none"> Immunosuppressant medication is contraindicated or has resulted in unacceptable 	<p>RANZCO and confirm the required approach to diagnosis and previous treatments.</p> <p>Valid contraindication reasons to immunosuppressant medication include</p> <ul style="list-style-type: none"> Significant infection including sepsis Potential for life threatening infection Pregnancy Marrow suppression and /or cytopenia Steroid induced side effects or Significant toxicity.

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		side effects or significant toxicity	
Review Criteria		<p>Review by a specialist in collaboration with an Ophthalmologist is required within 3 months of treatment to determine whether the patient has responded, and annually thereafter.</p> <p>Documentation of clinical effectiveness is necessary for continuation of IVIg therapy.</p> <p>On review of the initial authorisation period</p> <p>Clinical effectiveness of Ig therapy can be demonstrated by:</p> <ul style="list-style-type: none"> Improvement in visual function or an arrest in the decline of visual function as determined by an Ophthalmologist <p>On review of a continuing authorisation period</p> <p>For stable patients on maintenance treatment, review by an Ophthalmologist in collaboration with the treating specialist is required at least annually.</p> <p>Clinical effectiveness of Ig therapy can be demonstrated by:</p> <ul style="list-style-type: none"> Improvement in visual function or an arrest in the decline of visual function as determined by an Ophthalmologist 	<p>Review criteria drafted following consultation with RANZCO and confirm a treatment period of three months prior to assessing initial clinical response. Since ophthalmologists rarely prescribe intravenous immunoglobulins, they have indicated support for collaborative care with another specialist in all cases. They recommend that the treating ophthalmologist consults the collaborating specialist with regard to dosing with the treating ophthalmologist providing assessments of disease activity, severity and progression.</p> <p>RANZCO have advised that the continued use of intravenous immunoglobulin would be justified if function were to improve or if decline were to be halted. Long term use of intravenous immunoglobulin may be required in cases where cessation of treatment is accompanied by disease progression.</p>
Dose	Recommended dose is 1.5 g/kg/month for three months, with	<p>Induction Dose – 1.5g/kg in divided dose over 3 days</p> <p>Maintenance Dose – 0.4 to 1.5 g/kg in single or divided</p>	Induction and maintenance doses have been defined

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	<p>further maintenance dependent upon evidence of significant improvement in visual acuity and ocular inflammation.</p> <p>Dosing above 1 g/kg per day is contraindicated for some IVIg products.</p> <p>Refer to the current product information sheet for further information.</p> <p>The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.</p>	<p>doses monthly.</p> <p>The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.</p> <p>Refer to the current product information sheet for further information on dose, administration and contraindications.</p>	
<p style="text-align: center;">References</p> <p style="text-align: center;">(most recent update: Month YYYY)</p>			
<p>Castiblanco C and Foster CS, (2014) Review of Systemic Immunosuppression for Autoimmune Uveitis. <i>Ophthalmol Ther</i>, 3:17-36. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4254861/</p> <p>Garcia-Geremias M, Carreño E, Epps SJ, Lee RW and Dick AD (2015) Clinical outcomes of intravenous immunoglobulin therapy in refractory uveitis. <i>Int Ophthalmol.</i>; 35:281-5. https://www.ncbi.nlm.nih.gov/pubmed/25708281</p>			

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POTENTIAL OPERATIONAL IMPACT	
These criteria are largely thought to reflect current clinical practice and minimal operational impact is anticipated. While there will be some data entry required at initial Ig request and review, the clinical assessments are largely presented as drop down menus and short descriptions so as not to be burdensome	
POTENTIAL IMPACT ON PATIENTS, DEMAND AND EXPENDITURE	
Description of impact on patients:	<p>There is not anticipated to be any significant impact on patients given that these criteria align with the current clinical management of patients with this very rare condition and existing patients with proven AIR on Ig therapy will continue to receive Ig treatment. These criteria have been developed in consultation with Royal Australian and New Zealand College of Ophthalmologists and they have advised that Ig therapy is only required in severe cases where eye sight is threatened. The low level of Ig use over the last five years is consistent with this expected clinical practice.</p> <p>The formal access criteria now proposed for this condition require that an Ophthalmologist makes the diagnosis and manages the ongoing treatment in association with another treating specialist. This is because this is a very rare condition and it is important that the correct diagnosis is made and treatment given. There are a number of treatments that are available for this condition. Ig therapy is only used after patients have not responded to other treatments (unless they are unavailable or inappropriate).</p> <p>Existing patients will require annual checks by their Ophthalmologist to confirm that the visual function is improving or not worsening in response to the Ig therapy. Patients will already be reviewed regularly by their ophthalmologist so this requirement will not place an added burden on patients. If visual function is worsening, Ig therapy will be stopped and an alternative treatment approach will be used. It is acknowledged that some patients may require long term treatment to maintain their eyesight.</p> <p>New patients authorised to receive Ig therapy will require an initial check after three months Ig treatment to confirm that Ig therapy is improving eyesight and disease. If patients have not demonstrated a response after this time, Ig therapy will be ceased and substituted with a different treatment approach. If improvement has been demonstrated, annual checks on progress to assess the effectiveness of Ig maintenance therapy can be performed as part of the specialist's usual monitoring process.</p>
Impact on Demand	Based on the prescribing experience of Ophthalmologists with particular expertise in uveitis, the usage data indicating that Ig is used in less than 5 patients/year with Autoimmune Retinopathy (AIR) has been confirmed as being appropriate and in line with expected prevalence. Given that these criteria are in line with current clinical practice, there is not expected to be any impact on demand as a result of these changes.

PUBLIC CONSULTATION 2017 – Autoimmune retinopathy (previously Autoimmune uveitis)

	2011-12	2012-13	2013-14	2014-15	2015-16	The Specialist Working Group estimated magnitude of effect: No impact against projected demand
Patient number	0	<5	<5	<5	<5	
Total Grams issued	0	<500	<500	<1000	<1000	
% Total Grams issued	0.0%	<0.02%	<0.01%	<0.03%	<0.02%	
Specialist Working Group knowledge development opportunities and recommendations						
None identified at this stage.						

END OF PUBLIC CONSULTATION DOCUMENT

Next review: Eighteen months after Implementation of BloodSTAR v3.0