

Proposed changes to the *Criteria for the clinical use of intravenous immunoglobulin in Australia, Second Edition*

ITEM	CRITERIA FOR THE CLINICAL USE OF INTRAVENOUS IMMUNOGLOBULIN IN AUSTRALIA, SECOND EDITION (CRITERIA)	PROPOSED REVISIONS TO THE CRITERIA	SWG RATIONALE FOR PROPOSED CHANGE (A) Administrative (B) Progressive (C) Programmed
Condition Name	Idiopathic (autoimmune) thrombocytopenic purpura (ITP) — adult	Immune thrombocytopenic purpura (ITP) — adult	<a href="#">Change in condition name.</a>
Specialty	Haematology	Haematology	
Chapter	5	5	
Specific Conditions		<a href="#">Newly Diagnosed ITP</a> <a href="#">Persistent ITP</a> <a href="#">Chronic ITP</a>  Evans Syndrome - autoimmune haemolytic anaemia (AIHA) with immune thrombocytopenia	<a href="#">Revised terminology introduced for phase of disease as defined by the International Working Party on ITP. The use of specific conditions will support data analysis by phase of disease.</a>  Evans syndrome no longer exists as a separate condition and will be accessed under ITP- adult and ITP – children or AIHA.
Level of Evidence	Evidence of probable benefit ( <a href="#">Category 2a</a> ).	Evidence of probable benefit ( <a href="#">Category 2a</a> ).	
Description and Diagnostic Criteria	ITP is a reduction in platelet count (thrombocytopenia) resulting from shortened platelet survival due to anti-platelet antibodies. When counts are very low (<30x10 <sup>9</sup> /L), bleeding into the skin (purpura) and mucous membranes can occur. Bone marrow platelet production (megakaryopoiesis) is morphologically normal. In some cases, there is additional impairment of platelet function related to antibody binding to	ITP is a reduction in platelet count (thrombocytopenia) resulting from shortened platelet survival due to anti-platelet antibodies, <a href="#">reduced platelet production due to immune-induced reduced megakaryopoiesis and/or immune mediated direct platelet lysis</a> . When counts are very low (<30 x 10 <sup>9</sup> /L), bleeding into the skin (purpura) and mucous membranes can occur. Bone marrow platelet production	<a href="#">Improvements made to the description of the pathogenesis.</a>

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	<p>glycoproteins on the platelet surface. ITP is divided into chronic and acute forms. It is a common finding in patients with HIV, and while it may be found at any stage of the infection, its prevalence increases as HIV disease advances.</p> <p>Around 80% of adults with ITP have the chronic form of disease. The highest incidence of chronic ITP is in women aged 15–50 years, although some reports suggest increasing incidence with age.</p> <p>Chronic ITP may relapse and remit spontaneously and the course may be difficult to predict. If the platelet count can be maintained at a level that prevents spontaneous bleeding or bruising, the outlook is good.</p>	<p>(megakaryopoiesis) is morphologically normal. In some cases, there is additional impairment of platelet function related to antibody binding to glycoproteins on the platelet surface. ITP is divided into chronic and acute forms. It is a common finding in patients with human immunodeficiency virus (HIV), and while it may be found at any stage of the infection, its prevalence increases as HIV disease advances.</p> <p>Around 80% of adults with ITP have the chronic form of disease. The highest incidence of chronic ITP is in women aged 15–50 years, although some reports suggest increasing incidence with age.</p> <p>Chronic ITP may relapse and remit spontaneously and the course may be difficult to predict. If the platelet count can be maintained at a level that prevents spontaneous bleeding or bruising, the outlook is good.</p> <p><u>The International Working Group, terminology for the phases and severity of ITP disease are used in these Criteria.</u> <u>Newly diagnosed is used for all cases within 3 months of diagnosis; Persistent ITP relates to</u></p>	<p><u>Revised terminology is described and includes definitions of phases of disease.</u></p>

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		<p><u>patients not achieving spontaneous remission within 3 to 12 months from diagnosis or not maintaining a response to treatment during this time ; Chronic ITP indicates patients with ITP lasting greater than 12 months.</u></p> <p><u>Severe ITP relates to patients with clinically relevant bleeding mandating treatment or new bleeding mandating a change in therapy.</u></p> <p><u>In the context of these Criteria, Refractory refers to patients where splenectomy has failed to correct the ITP or splenectomy is contraindicated and second line therapy has been unsuccessful.</u></p> <p>Evans syndrome is a rare but serious autoimmune disease defined by the simultaneous or sequential occurrence of AIHA and immune thrombocytopenia purpura (ITP) without underlying aetiology. As such, it is a diagnosis of exclusion and other disorders, such as collagen vascular diseases, especially systemic lupus erythematosus (SLE) and scleroderma should be ruled out. The 2005 review by Norton and Roberts provided perspective on diagnosis, clinical features and management.</p>	

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<b>Justification for Evidence Category</b>	<p>Five small prospective studies, including three randomised studies, demonstrated equivalent efficacy of IVIg in comparison to prednisone 1 mg/kg/ day and high-dose dexamethasone regimen. Overall, the studies found a dose response with more rapid increment in platelet counts at scheduling <math>\geq 0.8</math> g/kg on day one compared with 0.4 g/kg/day for three days.</p> <p>A small controlled study (10 patients in each arm) of HIV-positive patients with severe thrombocytopenia reported possible benefit for the restoration and maintenance of platelet count for the duration of the haemorrhagic disorder (Biotext 2004).</p> <p>An international consensus statement from January 2010 (Provan et al 2010) reported on new data and provided consensus-based recommendations relating to diagnosis and treatment of ITP in adults, in children, and during pregnancy. This statement concluded that few RCTs have been conducted and that multi-centre, prospective RCTs are required.</p>	<p>Five small prospective studies, including three randomised studies, demonstrated equivalent efficacy of intravenous immunoglobulin (IVIg) in comparison to prednisone 1 mg/kg/ day and high-dose dexamethasone regimen. Overall, the studies found a dose response with more rapid increment in platelet counts at scheduling <math>\geq 0.8</math> g/kg on day one compared with 0.4 g/kg/day for three days.</p> <p>A small controlled study (10 patients in each arm) of HIV-positive patients with severe thrombocytopenia reported possible benefit for the restoration and maintenance of platelet count for the duration of the haemorrhagic disorder (Biotext 2004).</p> <p>An international consensus statement from January 2010 (Provan et al 2010) reported on new data and provided consensus-based recommendations relating to diagnosis and treatment of ITP in adults, in children, and during pregnancy. This statement concluded that few randomised controlled trials (RCTs) have been conducted and that multi-centre, prospective RCTs are required.</p>	

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		<p>A 2005 review on the management of Evans syndrome, based on Massachusetts Hospital data and a literature review, showed a transient response in all patients unless IVIg was given every three weeks (Norton and Roberts 2006). The review concluded that the data supported a role for IVIg in first-line therapy. It was not clear whether it was important for steroids to be given at the same time, although this is common practice. A total dose of 2 g/kg in divided doses appeared to be sufficient. The review also stated that there might be a role for IVIg in preference to steroids in the acute setting in very young children.</p> <p>A recent meta-analysis of low to medium quality evaluated outcomes of 13 small RCTs comparing high dose (2g/kg) to lower dose (1g/kg) IVIg in acute ITP. The analysis demonstrated equivalent efficacy for all endpoints studied including platelet responses and control of bleeding (Qin YH et al 2010) in both high dose and low dose groups.</p>			
<b>Diagnosis is required</b>	Refractory acute ITP <i>on the recommendation of a clinical haematologist</i>	Yes	Which Speciality	Haematologist, Paediatrician or General Physician	Specialties of treating specialists are required to be identified within the Ig system. (A)

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Diagnosis must be verified		No	Which Specialty	
Exclusion Criteria				
Indication for use	<p><b>1. Refractory acute ITP on the recommendation of a clinical haematologist</b></p> <p>Patients with severe thrombocytopenia (platelets <math>&lt;30 \times 10^9/L</math>) who have not responded to corticosteroid therapy.</p> <p><b>2. ITP with life-threatening haemorrhage or the potential for life-threatening haemorrhage</b></p> <p>Patients with severe thrombocytopenia (<math>&lt;30 \times 10^9/L</math>) with clinical evidence of a haemostatic defect (e.g. mucous membrane haemorrhage) or active bleeding.</p> <p><b>3. ITP in pregnancy</b></p> <p>a. Platelets <math>&lt;30 \times 10^9/L</math></p> <p>b. Impending delivery</p> <p><b>4. Specific circumstances</b></p> <p>a. Planned surgery</p>	<p><b><u>Newly diagnosed</u> ITP — initial <u>Ig</u> therapy.</b></p> <p><b>ITP in pregnancy - Initial <u>Ig</u> therapy.</b></p> <p><b>ITP with life-threatening haemorrhage or the potential for life-threatening haemorrhage.</b></p> <p><b><u>Newly diagnosed or persistent ITP – subsequent Ig therapy (Diagnosis &lt;12 months)</u></b></p> <p><b>Refractory <u>persistent</u> or chronic ITP — splenectomy failed or contraindicated and second-line agent unsuccessful.</b></p> <p><b>Ongoing treatment for ITP responders during pregnancy and the postpartum period.</b></p> <p><b>ITP and inadequate platelet count for planned surgery.</b></p> <p><b>HIV-associated ITP.</b></p>		<p><u>Indications have been revised in line with the changed terminology for phases of disease. The order of indications has been changed to ensure that the correct indication is selected for pregnancy.</u></p> <p><u>A new indication for managing ITP in the first twelve months has been introduced and the indication for Severe ITP is no longer required, as the meaning of ‘severe’ is now related to bleeding and not low platelet count. Refractory persistent and chronic ITP have been merged into a single indication given that the qualifying criteria and review are identical.</u></p> <p>ITP in pregnancy has each been split into 2 indications to support initial treatment and then ongoing therapy in those patients that have been shown to respond and require ongoing treatment.</p>

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	<p>b. Other concurrent risk factors for bleeding (e.g. concurrent anti-coagulant therapy)</p> <p>c. Severe ITP (platelets <math>&lt;30 \times 10^9/L</math>) where corticosteroids and immunosuppression are contraindicated</p> <p>d. Chronic ITP under the guidance of a clinical haematologist, as adjunctive therapy or where other therapies have failed or are not appropriate</p> <p><b>5. HIV-associated ITP</b></p> <p>Patients with severe ITP associated with HIV infection.</p>		
Qualifying Criteria	<p><b>1. Refractory acute ITP:</b></p> <p>1. Patients qualify for initial IVIg therapy when conventional doses of corticosteroids (0.5-2.0 mg/ kg prednisolone, or equivalent) have failed to improve the platelet count or stop bleeding within a clinically appropriate time frame, as assessed by a clinical haematologist. The objective of therapy is to induce a prompt increase in the</p>	<p><b><u>Newly diagnosed ITP — initial Ig therapy.</u></b></p> <ul style="list-style-type: none"> <li><u>Clinically significant bleeding and the current platelet count is less than <math>30 \times 10^9/L</math> or there is a risk of clinically significant bleeding and the platelet count is less than <math>30 \times 10^9/L</math></u></li> </ul> <p>AND</p> <ul style="list-style-type: none"> <li>There has been no improvement in response to conventional doses of corticosteroid therapy for at least 14 days (unless valid reason is provided) or corticosteroid therapy is contraindicated.</li> </ul>	<p><u>The qualifying criteria have been revised to focus on clinically significant bleeding or the risk of significant bleeding together with a very low platelet count.</u></p> <p>Evidence items supporting the eligibility criteria are formalised for each indication, eg failure to respond to steroid therapy is defined as being after 14 days treatment unless there is a valid reason. <u>Feedback was received regarding the timeframes required for steroid therapy, however, given that a valid reason can be recorded for not treating for 14 days, this has not been changed.</u></p> <p>Data will be captured on all alternative therapies</p>

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	<p>platelet count (to <math>&gt;30 \times 10^9/L</math>) while other therapies are introduced.</p> <p>2. Patients qualify for continuing doses when splenectomy has failed or is contraindicated AND where therapy with at least one second-line agent has been unsuccessful in maintaining a platelet count <math>&gt;30 \times 10^9/L</math>.</p> <p>With ongoing therapy, IVIg may be administered to achieve a platelet count <math>&gt;30 \times 10^9/L</math>. Further doses may be administered in responsive patients for up to 6 months (thereafter see <a href="#">Chronic refractory ITP</a>). The frequency and dose should be titrated to maintain a platelet count of at least <math>30 \times 10^9/L</math>. The objective of therapy is to maintain a safe platelet count while other therapeutic options are explored.</p> <p><b>2. ITP with life-threatening haemorrhage or the potential for life-threatening haemorrhage:</b></p> <p>IVIg therapy may be given when conventional doses of corticosteroids have failed or in conjunction with steroids when a rapid response is required.</p>	<p><b>ITP in pregnancy - Initial Ig therapy</b></p> <p>IVIg therapy is used to avoid corticosteroids, immunosuppressive agents and splenectomy during pregnancy. Once responder status has been demonstrated, doses titrated to maintain a platelet count <math>&gt; 30 \times 10^9/L</math> may be administered every three to four weeks throughout pregnancy.</p> <ul style="list-style-type: none"> <li>• Pregnant women are eligible when the current platelet count represents potential risk: <ul style="list-style-type: none"> <li>○ <math>&lt;30 \times 10^9/L</math> with risk of haemorrhage</li> <li>○ <math>&lt; 80 \times 10^9/L</math> with life-threatening haemorrhage or</li> <li>○ <math>&lt;100 \times 10^9/L</math> and impending delivery.</li> </ul> </li> </ul> <p><b>ITP with life-threatening haemorrhage or the potential for life-threatening haemorrhage.</b></p> <ul style="list-style-type: none"> <li>• IVIg therapy may be given to patients with life-threatening bleeding or potential for life threatening bleeding and the current platelet count is:</li> </ul>	<p>used and contraindication reason to steroids and immunosuppressive therapy are required to be provided. (A)</p> <p>Steroid contra-indication reasons include</p> <ul style="list-style-type: none"> <li>• Unstable Diabetes</li> <li>• Psychosis or mood disorder</li> <li>• Significant infection including sepsis</li> <li>• Severe osteoporosis</li> <li>• Myopathy</li> <li>• History of avascular necrosis</li> </ul> <p><u>An error was noted in the documents for public consultation and in response to feedback, ranges have been removed from the qualifying platelet counts and a maximum level has now been defined.</u></p>



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	<p><b>4. Specific circumstances:</b></p> <p>1. Planned surgery: IVIg may be used to achieve a platelet count considered safe for surgery. The safe threshold will vary with the nature of the surgery <i>(Recommended platelet counts for patients without concurrent risks of bleeding: minor dental work &gt;30x10<sup>9</sup>/L, minor surgery &gt;50x10<sup>9</sup>/L, major surgery &gt;80x10<sup>9</sup>/L, major neurosurgery &gt;100x10<sup>9</sup>/L.)</i></p> <p>2. Severe ITP: IVIg may be used where corticosteroids and immunosuppression are contraindicated.</p> <p><u>3.</u> Chronic refractory ITP unresponsive to all other available therapies: These patients may be considered for long-term maintenance therapy with IVIg, subject to regular review by a haematologist.</p>	<p>splenectomy failed or contraindicated and second-line agent unsuccessful.</p> <ul style="list-style-type: none"> <li><u>Clinically significant bleeding in a patient with Persistent or Chronic ITP and a current platelet count &lt;30 x 10<sup>9</sup>/L or a risk of clinically significant bleeding with a current platelet count &lt; 30x10<sup>9</sup>/L</u></li> </ul> <p>AND</p> <ul style="list-style-type: none"> <li><u>Response to Ig treatment demonstrated resolution of active bleeding or a reduction in evidence of bleeding correlating with a doubling of baseline platelet count and/or an increment in platelet count of greater than 10x10<sup>9</sup>/L within 7 days</u></li> </ul> <p>OR</p> <ul style="list-style-type: none"> <li><u>In patients without active bleeding a doubling of baseline platelet count and a rise in platelet count &gt; 30 x 10<sup>9</sup>/L was demonstrated within 7 days of previous Ig therapy</u></li> </ul> <p>AND</p> <ul style="list-style-type: none"> <li>Splenectomy has failed to correct thrombocytopenia or splenectomy is contraindicated.</li> </ul> <p>AND</p> <ul style="list-style-type: none"> <li>Therapy with a second-line agent has been unsuccessful in raising the platelet count above 30 x 10<sup>9</sup>/L.</li> </ul> <p>With ongoing therapy, IVIg may be</p>	<p><u>Qualifying criteria were amended to change the focus to bleeding or the risk of bleeding in the context of a very low platelet count.</u></p> <p><u>Feedback was received regarding the strictness of the IWG definition of response (previously 72 hours) noting that some patients may respond but take up to 7 days. The criteria for response were amended to define different requirements in the context of active bleeding or not.</u> (B)</p> <p>International working party on ITP have defined chronic ITP to commence after at least 12 months. The current version of criteria was based on 6 months. (A)</p> <p>Splenectomy contraindication reasons include extramedullary haematopoiesis and surgical contraindications. (A)</p> <p>Second line agent therapy includes</p> <ol style="list-style-type: none"> <li>Azathioprine</li> <li>Danazol</li> <li>Dapsone</li> <li>Rituximab</li> <li>TPO</li> <li>Other</li> </ol> <p>(A)</p>

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		<p>administered to achieve a platelet count of <math>&gt;30 \times 10^9/L</math>.</p> <p><b>Ongoing treatment for ITP responders during pregnancy and the postpartum period.</b> IVIg therapy is used to avoid corticosteroids, immunosuppressive agents and splenectomy during pregnancy. Further doses titrated to maintain a platelet count <math>&gt;30 \times 10^9/L</math> may be administered every three to four weeks throughout pregnancy.</p> <ul style="list-style-type: none"> <li>• Pregnant women are eligible when the current platelet count represents potential risk: <ul style="list-style-type: none"> <li>○ <math>&lt;30 \times 10^9/L</math> with risk of haemorrhage</li> <li>○ <math>&lt;80 \times 10^9/L</math> with life-threatening haemorrhage</li> <li>○ <math>&lt;100 \times 10^9/L</math> and impending delivery.</li> </ul> </li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• <u>Response to Ig treatment demonstrated resolution of active bleeding or a reduction in evidence of bleeding correlating with a doubling of baseline platelet count or an increment in platelet count of greater than <math>10 \times 10^9/L</math> within 7 days of previous Ig therapy</u> <b>OR</b></li> <li>• <u>In patients without active bleeding, a doubling of baseline platelet count and</u></li> </ul>	<p>Qualifying platelet counts for different scenarios have been defined. (A)</p> <p><u>An error was amended and the range of 80-100 for impending delivery was revised to the level of <math>&lt;100 \times 10^9/L</math>.</u></p> <p><u>Qualifying criteria defining responder status were amended as above.</u></p>

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	<p><b>5. HIV-associated ITP:</b></p> <p>1. Failure of antiretroviral therapy with platelet count <math>&lt;30 \times 10^9/L</math>;</p> <p>OR</p>	<p><u>a rise in platelet count <math>&gt; 30 \times 10^9/L</math> was demonstrated within 7 days of previous Ig therapy.</u></p> <p><b>ITP and inadequate platelet count for planned surgery.</b> IVIg may be used to achieve a platelet count considered safe for surgery. The safe threshold will vary with the nature of the surgery and whether there is a concurrent bleeding risk.</p> <ul style="list-style-type: none"> <li>• Patients are eligible when surgery is planned and platelet count is below the accepted cut-off for the intended surgery: <ul style="list-style-type: none"> <li>○ minor dental work (<math>&gt;30 \times 10^9/L</math>)</li> <li>○ major dental work (<math>&gt;50 \times 10^9/L</math>)</li> <li>○ minor surgery (<math>&gt;50 \times 10^9/L</math>)</li> <li>○ major surgery (<math>&gt;80 \times 10^9/L</math>)</li> <li>○ major neurosurgery (<math>&gt;100 \times 10^9/L</math>).</li> </ul> </li> </ul> <p><b>HIV-associated ITP.</b></p> <ul style="list-style-type: none"> <li>• <u>Failure of antiretroviral therapy and intracranial haemorrhage with a platelet count <math>&lt;80 \times 10^9/L</math></u></li> </ul> <p style="text-align: center;"><u>OR</u></p> <ul style="list-style-type: none"> <li>• <u>Failure of antiretroviral therapy and other life-threatening haemorrhage with a platelet count <math>&lt;50 \times 10^9/L</math></u></li> </ul>	<p><u>In response to feedback, the qualifying criteria were amended to improve the ease of comprehension.</u></p>

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	<p>2. Life-threatening haemorrhage secondary to thrombocytopenia.</p>	<p style="text-align: center;"><u>OR</u></p> <ul style="list-style-type: none"> <li>• <u>Failure of antiretroviral therapy and risk of clinically significant bleeding and platelet count &lt; 30x10<sup>9</sup>/L</u></li> </ul>	
<p><b>Review Criteria</b></p>	<ul style="list-style-type: none"> <li>• In chronic refractory ITP, six-month review assessing evidence of clinical benefit;</li> <li>• Resolution of bleeding;</li> <li>• Increment in platelet count.</li> </ul>	<p><b><u>Newly diagnosed</u> ITP — initial <u>Ig</u> therapy.</b></p> <p>Review Is not mandated for this indication however the following criteria may be useful in assessing the effectiveness of therapy.</p> <p><b>Outcome data to be measured</b></p> <ul style="list-style-type: none"> <li>○ <u>Resolution of active bleeding</u></li> <li>○ <u>A reduction in evidence of bleeding correlating with a doubling of platelet count or in platelet count &gt; 10<sup>9</sup>/L within 7 days</u></li> <li>○ <u>In patients without active bleeding a doubling of baseline platelet count and a rise in platelet count &gt; 30 x 10<sup>9</sup>/L was demonstrated within 7 days of previous Ig therapy</u></li> </ul> <p><b>Initial therapy for ITP in pregnancy.</b></p> <p>Review Is not mandated for this indication.</p>	<p>For one-off requests, patient outcome data can be entered but will not be mandatory.</p> <p><u>Outcome data have been amended in line with the revised criteria for responder status.</u></p> <p>Maintenance therapy is only supported for 3 indications – ongoing refractory ITP, pregnant Ig responders and chronic ITP (history of diagnosis now 12 rather than 6 months in line with ITPIWP).</p>

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		<p><b>ITP with life-threatening haemorrhage or the potential for life-threatening haemorrhage.</b></p> <p>Review is not mandated for this indication however the following criteria may be useful in assessing the effectiveness of therapy.</p> <p><b>Outcome data to be measured</b></p> <ul style="list-style-type: none"> <li>○ <u>Resolution of active bleeding</u></li> <li>○ <u>A reduction in evidence of bleeding correlating with a doubling of platelet count or in platelet count &gt; 10<sup>9</sup>/L within 7 days</u></li> <li>○ <u>In patients without active bleeding a doubling of baseline platelet count and a rise in platelet count &gt; 30 x 10<sup>9</sup>/L was demonstrated within 7 days of previous Ig therapy</u></li> </ul> <p><b><u>Newly diagnosed or persistent ITP – subsequent therapy (diagnosis &lt; 12 months)</u></b></p> <p><b><u>Review preamble</u></b></p> <p><u>Review must be undertaken six monthly by a haematologist.</u>  <u>Documentation of clinical effectiveness is necessary for continuation of IVIg therapy.</u></p> <p><u>Review criteria for assessing the effectiveness of IVIg use include:</u></p> <ul style="list-style-type: none"> <li>○ <u>Resolution of active bleeding</u></li> <li>○ <u>A reduction in evidence of bleeding</u></li> </ul>	<p><u>Outcome data have been amended in line with the revised criteria for responder status.</u></p> <p><u>Review of the new indication for the management in the first 12 months of ITP when ongoing therapy is required.</u></p> <p><u>Consistency has been applied in the definitions of responder status across all indications.</u></p>

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		<p><u>correlating with a doubling of baseline platelet count or an increment in platelet count &gt; 10<sup>9</sup>/L within 7 days</u></p> <ul style="list-style-type: none"> <li>○ <u>In patients without active bleeding a doubling of baseline platelet count and a rise in platelet count &gt; 30 x 10<sup>9</sup>/L was demonstrated within 7 days of previous Ig treatment.</u></li> </ul> <p><u>Ongoing use of IVIg should be primarily to prevent bleeding while other treatment options are explored, including splenectomy.</u></p> <p><b><u>On review of an authorisation request</u></b></p> <ul style="list-style-type: none"> <li>● <u>Patients qualify for continuing doses when the maintenance platelet count is less than 30 x 10<sup>9</sup>/L</u></li> </ul> <p><b><u>AND</u></b></p> <ul style="list-style-type: none"> <li>● <u>Response to Ig treatment demonstrated resolution of active bleeding or a reduction in evidence of bleeding correlating with a doubling of baseline platelet count or an increment in platelet count of greater than 10x10<sup>9</sup>/L within 7 days</u></li> </ul> <p style="text-align: center;"><b><u>OR</u></b></p> <ul style="list-style-type: none"> <li>● <u>In patients without active bleeding, a doubling of baseline platelet count and a rise in platelet count &gt; 30 x 10<sup>9</sup>/L was demonstrated within 7 days of previous Ig therapy</u></li> </ul> <p><b>Refractory <u>Persistent or Chronic ITP</u>—splenectomy failed or contraindicated and</b></p>	

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		<p><b>second-line agent unsuccessful.</b></p> <p>Review must be undertaken six monthly by a Haematologist. Documentation of clinical effectiveness is necessary for continuation of IVIg therapy.</p> <p>Review criteria for assessing the effectiveness of IVIg use include:</p> <ul style="list-style-type: none"> <li>○ <u>Resolution of active bleeding</u></li> <li>○ <u>A reduction in evidence of bleeding correlating with a doubling of baseline platelet count or an increment in platelet count &gt; 10<sup>9</sup>/L within 7 day</u></li> <li>○ <u>In patients without active bleeding a doubling of baseline platelet count and a rise in platelet count &gt; 30 x 10<sup>9</sup>/L was demonstrated within 7 days of previous Ig treatment</u></li> </ul> <p><b><u>On review of an authorisation request</u></b></p> <ul style="list-style-type: none"> <li>● <u>Patients qualify for continuing doses when the maintenance platelet count is &lt;30x10<sup>9</sup>/L</u></li> </ul> <p><b><u>AND</u></b></p> <ul style="list-style-type: none"> <li>● <u>Response to Ig treatment demonstrated resolution of active bleeding or a reduction in evidence of bleeding correlating with a doubling of baseline platelet count or an increment in platelet count of greater than 10x10<sup>9</sup>/L within 7 days</u></li> </ul> <p style="text-align: center;"><b><u>OR</u></b></p>	<p><u>Consistency has been applied in the definitions of responder status across all indications.</u></p>

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		<ul style="list-style-type: none"> <li>• <u>In patients without active bleeding a doubling of baseline platelet count and a rise in platelet count &gt; 30 x 10<sup>9</sup>/L was demonstrated within 7 days of previous Ig therapy</u></li> </ul> <p>The frequency and dose should be titrated to maintain a platelet count of at least 30 x 10<sup>9</sup>/L. The objective of therapy is to maintain a safe platelet count while other treatment options are explored.</p> <p><b>Ongoing treatment for ITP responders during pregnancy and the postpartum period.</b></p> <p>Review is not mandated for this indication however the following criteria may be useful in assessing the effectiveness of therapy. Maximum length of authorisation is 12 months.</p> <p><b>Outcome data to be measured</b> Review criteria for assessing the effectiveness of IVIg use include:</p> <ul style="list-style-type: none"> <li>○ <u>Resolution of active bleeding</u></li> <li>○ <u>A reduction in evidence of bleeding correlating with a doubling of platelet count or rise in platelet count &gt; 10<sup>9</sup>/L within 7 days</u></li> <li>○ <u>In patients without active bleeding a</u></li> </ul>	

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		<p><u>doubling of baseline platelet count and a rise in platelet count &gt; 30 x 10<sup>9</sup>/L was demonstrated within 7 days of previous Ig therapy</u></p> <p><b>ITP and inadequate platelet count for planned surgery.</b></p> <p>Review Is not mandated for this indication however the following criteria may be useful in assessing the effectiveness of therapy.</p> <p><b>Outcome data can be measured</b></p> <ul style="list-style-type: none"> <li>○ <u>Resolution of active bleeding</u></li> <li>○ <u>A reduction in evidence of bleeding correlating with a doubling of platelet count or rise in platelet count &gt; 10<sup>9</sup>/L within 7 days</u></li> <li>○ <u>In patients without active bleeding a doubling of baseline platelet count and a rise in platelet count &gt; 30 x 10<sup>9</sup>/L was demonstrated within 7 days of previous Ig therapy</u></li> </ul> <p>With ongoing therapy, IVIg may be administered to achieve a platelet count of &gt;30 x 10<sup>9</sup>/L.</p>	

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		<p><b>HIV-associated ITP.</b></p> <p>Review Is not mandated for this indication however the following criteria may be useful in assessing the effectiveness of therapy.</p> <p><b>Outcome data to be measured</b></p> <ul style="list-style-type: none"> <li>○ <u>Resolution of active bleeding</u></li> <li>○ <u>A reduction in evidence of bleeding correlating with a doubling of platelet count or rise in platelet count &gt; 10<sup>9</sup>/L within 7 days</u></li> <li>○ <u>In patients without active bleeding a doubling of baseline platelet count and a rise in platelet count &gt; 30 x 10<sup>9</sup>/L was demonstrated within 7 days of previous Ig therapy</u></li> </ul>	
<b>Dose</b>	<p><b>Initial therapy:</b> 1–2 g/kg as a single or divided dose.</p> <p><b>Ongoing therapy:</b> When indicated, 1–2 g/kg in single or divided dose at 4 to 6 weekly intervals titrated to symptoms and platelet count.</p> <p><b>Dosing above 1 g/kg per day is contraindicated for some IVIg products.</b></p> <p><b>Refer to the current product information sheet for further information.</b></p> <p><b>The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.</b></p>	<p><b><u>Newly diagnosed ITP</u> — initial <u>Ig</u> therapy.</b></p> <p><b>Induction Dose:</b> 1–2 g/kg as a single dose or divided dose.</p> <p>The objective of IVIg therapy in ITP is to maintain a safe platelet count while other therapeutic options are explored.</p> <p>The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.</p> <p>Dosing above 1g/kg per day is contraindicated for some IVIg products.</p>	<p>SWG observed that approach to dosing is variable amongst clinicians. Use of 1g/Kg as a single dose is more common than 0.4 g/Kg for 5 days (total dose 2g/Kg). When the patient is regionally based - 5 days of treatment will be approved, whereas in metro centres where imprest stock is available, 3 days at 0.4g/kg is approved. If patients have the first 3 days and have not responded then the Blood Service will approve the last 2 days.</p> <p>It was noted that there have been a couple of studies using 1g/kg however dosing with 1-2g/L is in line with published international guidelines and consensus statements for ITP.</p> <p>SWG discussion noted that the lower limit should be set to 0.4g/L for all conditions. The SWG noted that if a prescriber</p>

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		<p>Refer to the current product information sheet for further information.</p> <p><b>ITP in pregnancy - Initial <u>Ig</u> therapy.</b></p> <p><b>Induction Dose:</b> 1–2 g/kg as a single dose or divided dose. During pregnancy, further doses titrated to maintain a platelet count <math>&gt;30 \times 10^9/L</math> may be administered every three to four weeks throughout pregnancy. For impending delivery, IVIg therapy may be used to achieve a platelet count considered safe for delivery (<math>80\text{--}100 \times 10^9/L</math>).</p> <p>The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.</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><b>ITP with life-threatening haemorrhage or the potential for life-threatening haemorrhage.</b></p> <p><b>Induction Dose:</b> 1–2g /kg as a single dose or divided dose.</p> <p>The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.</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><b><u>Newly diagnosed or persistent ITP – subsequent therapy</u></b></p>	<p>tried to dose below the recommended minimum, an alert should advise that they are dosing below because prescribing should be at or above the minimum in this condition.</p>

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		<p><u>Maintenance dose: When indicated, 0.4–2 g/kg in single or divided dose at 4- to 6-weekly intervals titrated to symptoms and platelet count. A maximum dose of 2 g per month might be divided in lower doses more frequently. The objective of IVIg therapy in ITP is to maintain a safe platelet count while other therapeutic options are explored.</u></p> <p><u>The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient. Dosing above 1 g/kg per day is contraindicated for some IVIg products.</u></p> <p><u>Refer to the current product information sheet for further information.</u></p> <p><b>Refractory <u>persistent or chronic</u> ITP — splenectomy failed or contraindicated and second-line agent unsuccessful.</b></p> <p><b>Maintenance Dose:</b> When indicated, 0.4–2 g/kg in single or divided dose at 4- to 6-weekly intervals titrated to symptoms and platelet count. A maximum dose of 2 g per month might be divided in lower doses more frequently.</p> <p>The objective of IVIg therapy in ITP is to maintain a safe platelet count while other therapeutic options are explored.</p> <p>The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.</p> <p>Dosing above 1 g/kg per day is contraindicated for some IVIg products.</p> <p><b>Refer to the current product information sheet for</b></p>	

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		<p>further information.</p> <p><b>Ongoing treatment for ITP responders during pregnancy and the postpartum period.</b>  <b>Maintenance Dose:</b> When indicated, 0.4–2 g/kg in single or divided dose at 4- to 6-weekly intervals titrated to symptoms and platelet count. A maximum dose of 2 g per month might be divided in lower doses more frequently.</p> <p>The objective of IVIg therapy in ITP is to maintain a safe platelet count while other therapeutic options are explored.</p> <p>The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.</p> <p>Dosing above 1 g/kg per day is contraindicated for some IVIg products.</p> <p><b>Refer to the current product information sheet for further information.</b></p> <p><b>ITP and inadequate platelet count for planned surgery.</b></p> <p><b>Induction Dose:</b> 1–2 g/kg as a single or divided dose.</p> <p>IVIg may be used to achieve a platelet count considered safe for surgery.</p> <p>The safe threshold will vary with the nature of the surgery.</p> <p>The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.</p> <p>Dosing above 1 g/kg per day is contraindicated for some</p>	

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		<p>IVIg products.</p> <p><b>Refer to the current product information sheet for further information.</b></p> <p><b>HIV-associated ITP.</b></p> <p><b>Induction Dose:</b> 1–2 g/kg as a single dose or divided dose.</p> <p>The objective of IVIg therapy in ITP is to maintain a safe platelet count while other therapeutic options are explored.</p> <p>The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.</p> <p>Dosing above 1 g/kg per day is contraindicated for some IVIg products.</p> <p><b>Refer to the current product information sheet for further information.</b></p>	

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