

Immune thrombocytopenic purpura (ITP) — in children 15 years and younger

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Condition for which IVIg has an emerging therapeutic role.

Specific Conditions	<ul style="list-style-type: none">• ITP - child - newly diagnosed• ITP - child - persistent• ITP - child - chronic• Evans syndrome child - with significant ITP
Indication for IVIg Use	<ul style="list-style-type: none">• Treatment of life threatening bleeding in a child with ITP• Treatment of significant bleeding in newly diagnosed or persistent ITP with a platelet count less than $30 \times 10^9/L$• Treatment of moderate to severe bleeding in chronic ITP in responsive patients with platelet count less than $30 \times 10^9/L$ where other therapeutic options have failed or are contraindicated• Treatment to elevate platelet count to haemostatically safe levels prior to surgery in responsive patients with chronic ITP
Level of Evidence	Clear evidence of benefit (Category 1)
Description and Diagnostic Criteria	<p>Immune thrombocytopenic purpura (ITP) is a reduction in platelet count (thrombocytopenia) resulting from shortened platelet survival due to anti-platelet antibodies. When counts are very low ($<30 \times 10^9/L$), bleeding into the skin (purpura) and mucous membranes can occur. Bone marrow morphology is 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 three phases of disease: newly diagnosed (less than 3 months since diagnosis), persistent (greater than 3 months but less than 12 months) and chronic (greater than 12 months). In children, the newly diagnosed and persistent forms are the most common. The disease tends to present abruptly with dramatic evidence of bleeding into the skin (petechiae and purpura) and mucous membranes (gum bleeding, nose bleeds, blood blisters).</p> <p>Evans syndrome is a rare but serious autoimmune disease defined by the simultaneous or sequential occurrence of Autoimmune haemolytic anaemia (AIHA) and 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.</p> <p>The 2005 review by Norton and Roberts provided perspective on diagnosis, clinical features and management.</p> <p>Occurrence</p> <p>Girls and boys are affected equally. In 75% of patients, the episode follows vaccination or a viral infection such as varicella or infectious mononucleosis.</p> <p>Prognosis</p> <p>At least 80–90% of children will have spontaneous remission of their disease within 6–12 months. In 5–10% of cases, the disease may become chronic (lasting >12 months). Morbidity and mortality from newly diagnosed or persistent ITP is very low.</p>
Justification for Evidence Category	Category 1 classification in the Biotext (2004) review was based on four low–moderate quality randomised controlled trials (RCTs). The Frommer and Madronio

(2006) review identified a good-quality systematic review/meta-analysis of RCTs to support the [Category 1](#) classification.

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.

A recent meta-analysis of 13 small RCTs comparing high dose (2g/kg) to lower dose (1g/kg) IVIg in newly diagnosed/persistent ITP demonstrated equivalent efficacy for all endpoints including platelet responses and control of bleeding (Qin YH et al 2010).

Qualifying Criteria for IVIg Therapy

Treatment of life threatening bleeding in a child with ITP

- Life-threatening bleeding due to thrombocytopenia
- AND
- Current platelet count less than $50 \times 10^9/L$

Treatment of significant bleeding in newly diagnosed or persistent ITP with a platelet count less than $30 \times 10^9/L$

ITP is divided into three phases of disease: newly diagnosed (less than 3 months since diagnosis), persistent (greater than 3 months but less than 12 months) and chronic (greater than 12 months).

- Current platelet count is less than $30 \times 10^9/L$
- AND
- Moderate to severe mucosal and/or cutaneous bleeding

Treatment of moderate to severe bleeding in chronic ITP in responsive patients with platelet count less than $30 \times 10^9/L$ where other therapeutic options have failed or are contraindicated

ITP is divided into three phases of disease: newly diagnosed (less than 3 months since diagnosis), persistent (greater than 3 months but less than 12 months) and chronic (greater than 12 months).

- Current platelet count less than $30 \times 10^9/L$ in a patient with chronic ITP with previously demonstrated response to Ig therapy

AND

- Moderate to severe bleeding symptoms
- OR
- There is a risk of clinically significant bleeding

AND

- Other therapeutic options have failed
- OR
- Other therapeutic options are contraindicated

Treatment to elevate platelet count to haemostatically safe levels prior to surgery in responsive patients with chronic ITP

ITP is divided into three phases of disease: newly diagnosed (less than 3 months since diagnosis), persistent (greater than 3 months but less than 12 months) and chronic (greater than 12 months).

- Chronic ITP and previous documented response to Ig therapy

AND

- Pending surgery requiring haemostatically safe platelet count for relevant procedure:
 - minor dental work ($>30 \times 10^9/L$)
 - major dental ($>80 \times 10^9/L$)
 - minor surgery ($>50 \times 10^9/L$)
 - major surgery ($>80 \times 10^9/L$)
 - major neurosurgery ($>100 \times 10^9/L$)

Exclusion Criteria

Evans syndrome where predominant feature is AIHA - see [Autoimmune haemolytic anaemia \(AIHA\)](#)

**Review Criteria for Assessing
the Effectiveness of IVIg Use**

Treatment of life threatening bleeding in a child with ITP

Review is not mandated for this indication, however the following criteria may be useful in assessing the effectiveness of Ig therapy.

- Resolution of active bleeding, or reduction in evidence of bleeding correlating with a doubling of platelet count or a platelet count greater than $30 \times 10^9/L$ within 7 days of Ig therapy

Treatment of significant bleeding in newly diagnosed or persistent ITP with a platelet count less than $30 \times 10^9/L$

Review is not mandated for this indication, however the following criteria may be useful in assessing the effectiveness of Ig therapy.

- Resolution of active bleeding, or reduction in evidence of bleeding correlating with a doubling of platelet count or a platelet count greater than $30 \times 10^9/L$ within 7 days of Ig therapy

Treatment of moderate to severe bleeding in chronic ITP in responsive patients with platelet count less than $30 \times 10^9/L$ where other therapeutic options have failed or are contraindicated

Review must be undertaken six monthly by a haematologist, paediatrician, or general physician.

Documentation of clinical effectiveness is necessary for continuation of IVIg therapy.

Clinical effectiveness of Ig therapy may be demonstrated by:

On review of the initial authorisation period

- The platelet count responds to Ig therapy but cannot be maintained above $30 \times 10^9/L$

AND

- Ig therapy resulted in resolution of active bleeding, or a reduction in evidence of bleeding correlating with a doubling of platelet count or an increase in platelet count by an increment of greater than $10 \times 10^9/L$ within seven days of Ig therapy

OR

- In patients without active bleeding, a doubling of baseline platelet count and a rise in platelet count to greater than $30 \times 10^9/L$ was demonstrated within seven days of the most recent Ig therapy

On review of a continuing authorisation period

- The platelet count responds to Ig therapy but cannot be maintained above $30 \times 10^9/L$

AND

- Ig therapy resulted in resolution of active bleeding or a reduction in evidence of bleeding, correlating with a doubling of baseline platelet count or an increase in platelet count by increment of greater than $10 \times 10^9/L$ within seven days of Ig therapy

OR

- In patients without active bleeding, a doubling of baseline platelet count and a rise in platelet count to greater than $30 \times 10^9/L$ was demonstrated within seven days of previous Ig therapy

The objective of therapy is to maintain a safe platelet count while other treatment options are explored.

Treatment to elevate platelet count to haemostatically safe levels prior to surgery in responsive patients with chronic ITP

Review is not mandated for this indication, however the following criteria may be useful in assessing the effectiveness of Ig therapy.

- Resolution of active bleeding, or reduction in evidence of bleeding correlating with a doubling of platelet count or a platelet count greater than $30 \times 10^9/L$ within 7 days of Ig therapy

OR

- In patients without active bleeding a doubling of baseline platelet count and a rise in platelet count greater than $30 \times 10^9/L$ was demonstrated within 7 days of Ig therapy

Dose

Treatment of life threatening bleeding in a child with ITP

- **Initial therapy** - 0.8 g/kg as an initial dose

One repeat dose at 24 to 48 hours may be given if response is inadequate and symptomatic thrombocytopenia recurs, provided a total dose of 2g/kg is not exceeded. The duration of response to the initial dose is typically two to four weeks.

The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.

Refer to the current product information sheet for further information on dose, administration and contraindications.

Treatment of significant bleeding in newly diagnosed or persistent ITP with a platelet count less than $30 \times 10^9/L$

- **Initial therapy** - 0.8 g/kg given as an initial dose

One repeat dose at 24 to 48 hours may be given if response is inadequate and symptomatic thrombocytopenia recurs provided a total dose of 2g/kg is not exceeded. The duration of response to the initial dose is typically two to four weeks.

The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.

Refer to the current product information sheet for further information on dose, administration and contraindications.

Treatment of moderate to severe bleeding in chronic ITP in responsive patients with platelet count less than $30 \times 10^9/L$ where other therapeutic options have failed or are contraindicated

- **Initial therapy** - 0.8 g/kg given as an initial dose
- **Maintenance Dose** - 0.4–2g/kg in a single or divided dose at 4 to 6 weekly intervals titrated to symptoms and platelet count up to a maximum of 2g/kg/4 week period.

The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.

Refer to the current product information sheet for further information on dose, administration and contraindications.

Treatment to elevate platelet count to haemostatically safe levels prior to surgery in responsive patients with chronic ITP

- **Initial therapy** - 0.8 g/kg given as an initial dose.

The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.

Refer to the current product information sheet for further information on dose, administration and contraindications.

Bibliography

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