Immune thrombocytopenic purpura (ITP) — adult

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Condition for which IVIg has an established therapeutic role.

Specific Conditions	• ITP with life-threatening haemorrhage or potential life-threatening haemorrhage • ITP refractory acute • ITP in pregnancy • ITP in specific circumstances (surgery, other therapy contraindicated, chronic ITP, concurrent risk factors) • ITP associated with HIV
Indication for IVIg Use	• ITP with life-threatening haemorrhage or the potential for life-threatening haemorrhage. • Refractory acute ITP — severe thrombocytopenia (platelets <$30x10^9$/L) and no response to corticosteroid therapy. • Refractory acute ITP — splenectomy failed or contraindicated and second-line agent unsuccessful. • ITP in pregnancy — impending delivery. • ITP in pregnancy — platelets <$30x10^9$/L. • Planned surgery with ITP and inadequate platelet count. • Severe ITP (platelets <$30x10^9$/L) where corticosteroids and immunosuppression are contraindicated. • Chronic or persistent ITP under the guidance of a Clinical Haematologist, as adjunctive therapy, or where other therapies have failed or are not appropriate. • ITP with other concurrent risk factors for bleeding (e.g. concurrent anti-coagulant therapy) • HIV–associated ITP.
Level of Evidence	Evidence of probable benefit – more research needed (Category 2a)
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 (<$30x10^9$/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 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) disease, and while it may be found at any stage of the infection, its prevalence increases as HIV disease advances. 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. 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.
Justification for Evidence Category	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 ≥0.8 g/kg on day one compared with 0.4 g/kg/day for three days.

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).

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.

Qualifying Criteria for IVIg Therapy

ITP with life-threatening haemorrhage or the potential for life-threatening haemorrhage.

A trial of 14 days with corticosteroid treatment is recommended. IVIg therapy may be given when conventional doses of corticosteroids have failed or in conjunction with steroids when a rapid response is required, where the platelet count is:

- <100 x 10^9/L in patients with intracranial haemorrhage
- <50 x 10^9/L in patients with other life-threatening haemorrhage
- <30 x 10^9/L in patients with a risk of haemorrhage.

- Life-threatening bleeding or the potential for life-threatening bleeding.

  AND
- Evidence of thrombocytopenia.

AND

- Conventional dose of corticosteroids has failed.

  OR
- A rapid response is required

  OR
- Corticosteroids are contraindicated

Refractory acute ITP — severe thrombocytopenia (platelets <30x10^9/L) and no response to corticosteroid therapy.

- Ig therapy recommended by a clinical haematologist

AND

- Current platelet count is less than 30x10^9/L.

AND

- No response to conventional doses of corticosteroid therapy.

A trial of 14 days with corticosteroid treatment is recommended.

Refractory acute ITP — splenectomy failed or contraindicated and second-line agent unsuccessful.

- Ig therapy recommended by a clinical haematologist

AND

- Current platelet count is less than $30x10^9$/L.

AND

- Splenectomy has failed to improve the platelet count.

  OR

- Splenectomy is contraindicated.

AND

- Therapy with a second-line agent has been unsuccessful in raising the platelet count above $30x10^9$/L.

With ongoing therapy, IVIg may be administered to achieve a platelet count of greater than $30x10^9$/L.
Further doses may be administered in responsive patients for up to 6 months (thereafter, see refractory chronic or persistent ITP).

ITP in pregnancy — impending delivery.

- To achieve a platelet count considered safe for delivery (80–$100x10^9$/L).

ITP in pregnancy — platelets <$30x10^9$/L.

Ig 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 greater $30x10^9$/L may be administered every three to four weeks throughout pregnancy.

- Current platelet count is less than $30x10^9$/L.

Planned surgery with ITP and inadequate platelet count.

- Platelet count is below that which is considered safe for 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 and whether there is a concurrent bleeding risk. Recommended platelet counts for patients without concurrent risks of bleeding:
  - minor dental work (>$30x10^9$/L)
  - major dental work (>$50x10^9$/L)
  - minor surgery (>$50x10^9$/L)
  - major surgery (>$80x10^9$/L)
  - major neurosurgery (>$100x10^9$/L).

Severe ITP (platelets <30x10^9/L) where corticosteroids and immunosuppression are contraindicated.

- Platelet count <30x10^9/L.

  AND

- Corticosteroids and immunosuppressant therapies are contraindicated.

Chronic or persistent ITP under the guidance of a Clinical Haematologist, as adjunctive therapy, or where other therapies have failed or are not appropriate.

- Ig therapy recommended by a clinical haematologist

AND

- Refractory chronic or persistent ITP (at least 6 months from the first diagnosis of ITP), with platelet count <30x10^9/L.

AND

- Conventional doses of steroids and second-line agents have failed to maintain the platelet count above 30x109/L.

  OR

- Immunosuppressant therapy is contraindicated.

AND

- Splenectomy has failed to adequately improve the low platelet count.

  OR

- Splenectomy is contraindicated.

ITP with other concurrent risk factors for bleeding (e.g. concurrent anti-coagulant therapy)

- Presence of other risk factors for bleeding.

AND

- Platelet count less than 50 x 10^9/L

HIV–associated ITP.

- Failure of antiretroviral therapy and platelet count of <30x10^9/L.

  OR

- There is a risk of life-threatening haemorrhage secondary to thrombocytopenia.

Review Criteria for Assessing the Effectiveness of IVIg Use	

ITP with life-threatening haemorrhage or the potential for life-threatening haemorrhage.

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

- Improvement in platelet count and a reduction in evidence of bleeding, if relevant.

Refractory acute ITP — severe thrombocytopenia (platelets <30x10^9/L) and no response to corticosteroid therapy.

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

- An improvement in the platelet count and a reduction in evidence of any bleeding.

Refractory acute ITP — splenectomy failed or contraindicated and second-line agent unsuccessful.

Review must be undertaken six-monthly by a Haematologist.

Review criteria for assessing the effectiveness of IVIg therapy include prevention/resolution of bleeding and an increment in platelet count.

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

On review of an authorisation period

- An improvement in platelet count post therapy and a reduction in evidence of bleeding

Further IVIg doses may be administered in responsive patients for up to 6 months (thereafter, see chronic refractory ITP).

The frequency and dose should be titrated to maintain a platelet count of at least 30x10^9/L.

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

ITP in pregnancy — impending delivery.

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

- An improvement in platelet count and a reduction in evidence of bleeding, if relevant.

ITP in pregnancy — platelets <30x10^9/L.

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

- An improvement in platelet count and a reduction in evidence of bleeding, if relevant.

Planned surgery with ITP and inadequate platelet count.

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

- An improvement in platelet count and a reduction in evidence of bleeding, if relevant .

Severe ITP (platelets <30x10^9/L) where corticosteroids and immunosuppression are contraindicated.

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

- An improvement in platelet count and a reduction in evidence of bleeding, if relevant.

Chronic or persistent ITP under the guidance of a Clinical Haematologist, as adjunctive therapy, or where other therapies have failed or are not appropriate.

Review must be undertaken six-monthly by a Haematologist.

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

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 of >30x10^9/L.

With ongoing therapy, IVIg may be administered to achieve a platelet count of >30x10^9/L.

On review of an authorisation period

- An improvement in platelet count and a reduction in evidence of bleeding.

Patients with chronic ITP may be considered for long-term therapy with IVIg, subject to regular review by a Haematologist.

ITP with other concurrent risk factors for bleeding (e.g. concurrent anti-coagulant therapy)

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

- An improvement in platelet count and a reduction in evidence of bleeding, if relevant.

HIV–associated ITP.

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

- An improvement in platelet count and a reduction in evidence of bleeding .

Dose

ITP with life-threatening haemorrhage or the potential for life-threatening haemorrhage.

- **Dose** - 1–2 g/kg as a single dose or divided dose.

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.

Refer to the current product information sheet for further information.

Refractory acute ITP — severe thrombocytopenia (platelets <30x10^9/L) and no response to corticosteroid therapy.

- **Dose** - 1–2 g/kg as a single dose or divided dose.

The objective of IVIg therapy in ITP is to maintain a safe platelet count while other therapeutic options are explored.

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.

Refer to the current product information sheet for further information.

Refractory acute ITP — splenectomy failed or contraindicated and second-line agent unsuccessful.

- **Initial Dose** - 1–2 g/kg in single or divided dose
- **Maintenance Dose** - When indicated, 1–2 g/kg in single or divided dose at four to six (4–6) weekly intervals titrated to symptoms and platelet count.

The objective of IVIg therapy in ITP is to maintain a safe platelet count while other therapeutic options are explored.

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.

Refer to the current product information sheet for further information.

ITP in pregnancy — impending delivery.

- **Dose** - 1–2 g/kg in single or divided dose. For impending delivery, IVIg therapy may be used to achieve a platelet count considered safe for delivery (80–100x10^9/L).

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.

Refer to the current product information sheet for further information.
Planned surgery with ITP and inadequate platelet count

ITP in pregnancy — platelets <30x10^9/L.

- **Induction Dose** - 1–2 g/kg as a single dose or divided dose.
- **Dose during pregnancy** - 1–2 g/kg as a single dose or divided dose. Further doses titrated to maintain a platelet count of >30x10^9/L may be administered every three to four weeks throughout pregnancy.

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.

Refer to the current product information sheet for further information.

Planned surgery with ITP and inadequate platelet count.

- **Dose** - 1–2 g/kg as a single or divided dose.

IVIg may be used to achieve a platelet count considered safe for surgery. The safe threshold will vary with the nature of the surgery.

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.

Refer to the current product information sheet for further information.

Severe ITP (platelets <30x10^9/L) where corticosteroids and immunosuppression are contraindicated.

- **Dose** - 1–2 g/kg as a single dose or divided dose.

The objective of IVIg therapy in ITP is to maintain a safe platelet count while other therapeutic options are explored.

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.

Refer to the current product information sheet for further information.

Chronic or persistent ITP under the guidance of a Clinical Haematologist, as adjunctive therapy, or where other therapies have failed or are not appropriate.

- **Maintenance Dose** - 1–2 g/kg in single or divided dose at four to six (4–6) weekly intervals titrated to symptoms and platelet count.

The objective of IVIg therapy in ITP is to maintain a safe platelet count while other therapeutic options are explored.

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.

Refer to the current product information sheet for further information.

ITP with other concurrent risk factors for bleeding (e.g. concurrent anti-coagulant therapy)

- **Initial Dose** - 1-2 g/kg as a single or divided dose.
- **Maintenance Dose** - Where indicated, 1-2 g/kg in a single dose or divided dose at 4 to 6 weekly intervals titrated to symptoms and platelet count.

The objective of IVIg therapy in ITP is to maintain a safe platelet count while other therapeutic options are explored.

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.

Refer to the current product information sheet for further information.

HIV–associated ITP.

- **Dose** - 1–2 g/kg as a single dose or divided dose.

The objective of IVIg therapy in ITP is to maintain a safe platelet count while other therapeutic options are explored.

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.

Refer to the current product information sheet for further information.

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