Tertiary/Quaternary Level Essential Drug List
Medication Review Summary

Medication Name: Human Intravenous Immune Globulin (IVIG) **Date:** July 2018

Indication: Immune thrombocytopenic Purpura (ITP), acute:

- Life-threatening bleed with platelets <50 x 10^9/l.
- Urgent surgery (any surgery urgently required within 24 hours) where rapid rise in platelets is required.
- Pregnant patient prior to delivery as above.
- Rapid rise in platelets required when a patient has platelet count of < 20 x 10^9/L, with additional risk factors for bleeding (such as severe hypertension, ongoing sepsis).

Context: ITP is an acquired thrombocytopenia caused by autoantibodies against platelet antigens occurring as a primary (idiopathic) process, or secondary to various other underlying conditions. ITP is a common condition with an incidence of 1 to 3 per 100 000 adults. Clinical presentation range from asymptomatic to severe life threatening bleeding. 20-30% of patients is asymptomatic. Intracranial haemorrhage (ICH) occur in 1.4%, and Non-IC severe bleeding in 9.6% of patients. 1st line therapy in adults is corticosteroids. Management of serious bleeding include pulsed high dose steroids (Dexamethasone 40mg x 4 days/Methylprednisolone 1g x 3 days), IVIG, and platelet transfusions.

Quality of evidence: Trials documenting the efficacy of IVIG date from the early 1980's. There is a paucity of randomized data, but clinical experience is extensive. IVIG is incorporated in all clinical guidelines on the management of ITP[1,2]. Evidence is graded as 1B in children, and 2B in adults[1].

Clinical efficacy: Compared to corticosteroids IVIG leads to a more rapid rise in platelet counts. Many respond within 24 hours (median 2-4 days), but responses are transient lasting 2 to 4 weeks[2].

Godeau et al[3] compared 0.7g/kg/day IVIG versus 15mg/kg methylprednisolone day 1 to 3 in 122 adults. Patients with platelet counts over 50 x 10^9/L on day 2 and 5 was 7% and 79% in the IVIG group versus 2% and 60% in the methylprednisolone group (p=0.04). Platelet counts was above 50 x 10^9/L for a median of 18 days versus 14 days in favour of IVIG.

In a separate study Godeau et al[4] compared 1g/kg versus 0.5g/kg IVIG in 40 consecutive adults with ITP. Non responders had a second infusion (to a total dose of 2g/kg). 12/18 patients responded by day 4 in 1g/kg group vs 4/19 in the 0.5g/kg group (p=0.005). Platelet counts were higher in the 1g/kg group on day 3 and day 4 (p=0.03).

Safety concerns: Infusion reactions including fever, chills, nausea and vomiting. Rarely anaphylactoid and hypersensitivity reactions. Acute renal failure in at risk individuals (e.g. volume depletion or pre-existing renal disease). Infection transmission.

Recommendation: IVIG is recommended *(in discussion with specialist with haemotological expertise)* in the above indications (in combination with pulse corticosteroid therapy and platelet transfusions for life threatening bleeds). The recommended dose in adults is 1g/kg as a single infusion that may be repeated once in non-responders. A single dose of 0.8g/kg to 1g/kg is recommended in children.
Note that platelet transfusions should be minimized as far as possible due to risk of allo-immunization.

IVIG is not recommended for the chronic treatment of ITP.

1. Neunert C et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood 2011 117:4190-4207
2. Provan D et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood 2010 115:168-186
3. Godeau B et al. Intravenous immunoglobulin or high-dose methylprednisolone, with or without oral prednisone, for adults with untreated severe autoimmune thrombocytopenic purpura: a randomized, multicenter trial. Lancet 2002; 359: 23-29
4. Godeau B et al. Intravenous immunoglobulin for adults with autoimmune thrombocytopenic purpura: results of a randomized trial comparing 0.5 and 1g/kg b.w. British Journal of Haematology 1999, 107, 716-719