BC Provincial Blood Coordinating Office

promoting good stewardship in transfusion medicine

Intravenous Immune Globulin (IVIg)

Utilization Management Program Recommendations

As per the BC Provincial Policy on Health Authority Immune Globulin Utilization Management and Ministry of Health Directives:

- Requests for IVIg to treat conditions on the "*List of Approved Medial Conditions for IVIg Use*" must be screened at the health authority or hospital level to ensure that any specific prerequisites have been met and that the dose and duration of therapy are in accordance with British Columbia IVIg Utilization Management Program guidelines.
- Use of IVIg for conditions not listed in the table below or in cases where the prerequisites are not met must be reviewed and approved at the discretion of a designated pathologist/hematopathologist who has expertise in the use of IVIg. Requests without appropriate evidence-based rationale may be rejected as per the Ministry of Health Directives.
- The maximum amount of IVIg administered should reflect adjusted body weight dosing in patients. Actual body weight will be used to determine dose for patients <18 years of age, weighing less than ideal body weight, patients under 153 cm (60 inches), and during pregnancy

List of Approved Medical Conditions for IVIg Use

Specialty	Medical Condition	Prerequisites / Comments	Dose and Duration
Immunology	Primary immune deficiency (PIDD)	▪ Hypogammaglobulinemia (reduced total IgG or IgG subclasses) with recurrent bacterial infection ▪ Monitor IgG trough level as appropriate to achieve desired clinical outcome	**Primary immune deficiency:** **Adults** based on severity of condition: Less severe: 0.2-0.4 g/kg every 3-4 weeks More severe: 0.4-0.6 g/kg every 3-4 weeks **Pediatric:** 0.4-0.6 g/kg every 3-4 weeks
	Secondary immune deficiency (SID)		**Secondary immune deficiency:** **Adult:** 0.4-0.6 g/kg every 3-4 weeks **Pediatric:** 0.3-0.6 g/kg every 4 weeks (*Currently under review*)
Hematology	Fetal-Neonatal alloimmune thrombocytopenia (F/NAIT)	▪ Previous affected pregnancy or family history of F/NAIT or mother found on screening to have platelet alloantibodies. IVIg is first-line treatment of FAIT. ▪ In newborn with NAIT the provision of antigen-negative compatible platelets should be first-line therapy and IVIg adjunctive. ▪ Treatment should be under the direction of a high-risk obstetrical centre with expertise in F/NAIT.	1-2 g/kg weekly, depending on gestational age and whether risk for complications of NAIT is standard or high
	Hemolytic disease of the newborn (HDN)	IVIg is indicated only in HDN infants with severe hyperbilirubinemia; i.e. TSB rising despite intensive phototherapy or TSB level within 34-51 micromol/L of the exchange level (TSB = total serum bilirubin)	0.5-1.0 g/kg. If necessary, dose may be repeated in 12 hours
	Idiopathic thrombocytopenic purpura (ITP) – pediatric	**Acute ITP:** IVIg may be considered initial therapy if the platelet count is <20 x 10^9/L. Consultation with a pediatric hematologist is advised. IVIg is recommended as part of multimodality therapy (with platelet transfusions and bolus intravenous MP) when the patient has life-threatening bleeding. IVIg is not indicated if only mild bleeding (petechiae, bruises or asymptomatic). **Chronic ITP:** IVIg may be considered.	**Acute ITP**: one dose of 0.8 to 1 g/kg, with a second dose within 48 hours if the platelet count has not increased to above 20 x 10^9/L **or** clinically significant bleeding persists requiring a higher platelet count
	Idiopathic thrombocytopenic purpura (ITP) – adult	▪ No treatment is required if the platelet count >20 x 10^9/L and there is no active bleeding **Acute ITP with bleeding:** IVIg is recommended as part of multimodality therapy for major or life-threatening bleeding complications and/or clinically important mucocutaneous bleeding. **Acute ITP with severe thrombocytopenia but no bleeding:** IVIg is not considered first-line therapy, except for patients with contraindications to steroids. **ITP with no/slow response to adequate dose steroids***:* IVIg may be considered as possible adjunctive therapy.	**Acute ITP:** one dose of 1 g/kg, with a second dose within 48 hours if the platelet count has not increased to above 20 x 10^9/L **or** clinically significant bleeding persists requiring a higher platelet count
Infectious Diseases	Staphylococcal toxic shock	▪ Evidence of systemic inflammation and end organ hypoperfusion with fever, tachycardia, tachypnea and hypotension ▪ Consult with medical microbiologist or infectious disease specialist before treatment	1 g/kg on day one and 0.5 g/kg per day on days two and three, **or** 0.15 g/kg per day over 5 days
	Invasive Group A streptococcal fasciitis with associated toxic shock		

List of Approved Medical Conditions for IVIg Use

Specialty	Medical Condition	Prerequisites / Comments	Dose and Duration
Infectious Diseases (cont'd)	Measles post-exposure prophylaxis	▪To prevent post-exposure measles disease in pregnant women, infants, and immunodeficient or immunosuppressed patients in whom weight (>30 kg) or ability to tolerate intramuscular (IM) injection precludes the use of an IM preparation of hyper immune globulin	0.4 g/kg as a single dose
Neurology	Guillain-Barré syndrome (GBS), including Miller-Fisher syndrome and other variants	▪Symptoms of grade 3 severity (able to walk with aid) or greater or symptoms less than grade 3 severity that are progressing ▪Treatment should be given within 2 weeks of symptom onset ▪Diagnosis of GBS variants should be made by a specialist with expertise in this area	**Adults:** 2 g/kg over 2-5 days **Pediatric**: 2 g/kg over 2 days
	Chronic inflammatory demyelinating polyneuropathy (CIDP)	▪IVIg is considered a first line treatment for initial treatment of CIDP. Some patients may respond fully to IVIg alone. ▪Other CIDP patients may have a limited or incomplete response to IVIg and then alternate treatments and immunosuppressants may be considered. ▪All patients receiving IVIg for chronic treatment of CIDP should be followed by a neuromuscular specialist.	**Initial treatment:** 2 g/kg over 2-5 days. **Maintenance therapy:** tailor to the lowest dose that maintains clinical efficacy, usually 0.5-1g/kg q 4-8 weeks. Continued use should be based on objective measures of sustained effectiveness
	Multifocal motor neuropathy (MMN)	Diagnosis should be made by a neuromuscular specialist, as very specific electrodiagnostic expertise is required	**Initial treatment:** 2 g/kg over 2-5 days. **Maintenance therapy:** tailor to the lowest dose that maintains clinical efficacy, 0.5-1 g/kg q 3-6 weeks.
	Myasthenia gravis (MG)	▪Severe exacerbations of MG or myasthenic crises, or to stabilize patients before surgery ▪IVIg is not recommended as maintenance therapy for patients with chronic MG	**Initial treatment:** 2 g/kg over 2-5 days, and if short term maintenance therapy is required, 0.5-1 g/kg q 3-4 weeks
Dermatology	Pemphigus vulgaris	▪Firm histological and immuno-diagnosis is needed. ▪Consider IVIg when there is no response or a contraindication to corticosteroids and immunosuppressive agents	2 g/kg over 5 days
Rheumatology	**IVIg use by patients over 18 years of age must be approved by the Rheumatology IVIg Consultant**		
	Juvenile dermatomyositis (JD)	Lack of response or contraindication to corticosteroids, Methotrexatate and/or Azathioprine therapy	**Initial treatment:** 2 g/kg over 2 days. **Maintenance therapy:** a systematic approach should be taken to determine minimum effective dose. Continued use should be based on objective measures of sustained effectiveness. Maximum dose per treatment course should not exceed 2 g/kg
	Kawasaki disease (KD)	Validity of diagnosis must be established	2 g/kg x 1 day Second dose may be given for patients who fail to respond the first time

IVIg is not recommended or is contraindicated for use in the following conditions:

- **Hematology**: aplastic anemia
- **Neurology**: adrenoleukodystrophy, amyotropic lateral sclerosis, autism, critical illness polyneuropathy, inclusion body myositis, intractable childhood epilepsy, paraproteinemic neuropathy (IgM variant), POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes)

References:

1) Anderson D et al. Guidelines on the use of intravenous immune globulin for hematologic conditions. Transfusion Medicine Reviews 2007(April);21(1,Suppl 1):S9-S56.
2) Feasby T et al. Guidelines on the use of intravenous immune globulin for neurologic conditions. Transfusion Medicine Reviews 2007(April);21(1,Suppl 1):S57-S107.
3) IVIg Utilization Management Handbook: First Edition. British Columbia Provincial Blood Coordinating Office, 2002.
4) Physician's Standing Order Request for IVIg – Recommended Dosing. Nova Scotia Provincial Blood Coordinating Program, 2004-05
5) National Advisory Committee on Immunization. Updated NACI recommendations for measles post-exposure prophylaxis. CCDR. 2018 Sept 6; 44(9): 226-230.