INESSS
LE SAVOIR PREND FORME

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INTRAVENOUS IMMUNOGLOBULIN (IVIg)

USE IN INFECTIOUS DISEASES

This optimal use guide is intended for infectious disease specialists and other medical specialists or physicians with expertise in treating patients with an infectious disease with IVIg. It is provided for information purposes only and should not replace the judgment of the clinician who performs activities reserved under an act or a regulation. The recommendations were developed using a systematic process and are supported by the scientific literature and the knowledge and experience of Québec clinicians and experts. For further details, go to inesss.qc.ca.

GENERAL INFORMATION

- Intravenous non-specific human immunoglobulin (IVIg) preparations are stable products derived from human plasma.
- Their use continued to increase in Québec in the past several years. Because of their high cost and the risk of a shortage, it is important to ensure that they are used judiciously.
- The price of one gram of IVIg is approximately $100 (2020). This price may vary, depending on the exchange rate for the Canadian dollar and the volume of fractionation plasma collected by Héma-Québec. The cost of IVIg for a 70-kg adult is approximately $14,000 for short-term therapy (at a total dose of 2 g/kg divided over 2 to 5 days).

INITIATING, MONITORING AND DISCONTINUING IVIg THERAPY

- Before initiating IVIg therapy:
  - The diagnosis should be confirmed by a physician with the necessary expertise or in consultation with a medical specialist;
  - The patient's free and informed consent must have been obtained and recorded in his or her medical record;
  - The patient's ideal weight should be calculated;
  - The patient's blood type should be determined, if it is not already indicated in his or her record.
- After IVIg therapy is initiated:
  - The tolerance and effectiveness of the therapy should be assessed by a physician with the necessary expertise or in consultation with a medical specialist.

RECOMMENDATIONS FOR USING IVIg BY INDICATION

A total of 10 infectious disease indications were evaluated (list not exhaustive).

IVIg A POSSIBLE TREATMENT OPTION

INDICATIONS	CONDITIONS OF USE
Pediatric viral cardiomyopathy[1]	▸ For children with severe acute viral myocarditis and in the presence of a decreased ejection fraction or significant cardiac dysfunction.
Toxic shock syndrome	▸ For patients with toxic shock syndrome, based on established diagnostic criteria. ▸ Always in combination with appropriate antibiotic therapy.
Multisystem inflammatory syndrome in children temporally associated with COVID-19[2]	▸ For children with multisystem inflammatory syndrome temporally associated with COVID-19, based on established diagnostic criteria.

1. Little or no data are available in the literature on the efficacy of Ig in pediatric viral myocarditis. This recommendation is therefore based on the consulted experts' clinical experience. Consultation with a pediatric cardiologist is necessary to assess the appropriateness of prescribing IVIg therapy.
2. Little data are available in the literature on the efficacy of Ig for this indication. This recommendation is therefore based on the consulted experts' clinical experience.

IVIg NOT RECOMMENDED

INDICATIONS
▸ Adult viral cardiomyopathy[3]
▸ COVID-19 (without multisystem inflammatory syndrome)
▸ *Clostridioides difficile* enterocolitis
▸ Sepsis (except neonatal enterovirus sepsis)
▸ *Mycoplasma pneumoniae*-induced rash and mucositis[4]
▸ Adult necrotizing fasciitis (without shock criteria)
▸ Infection prevention post trauma or surgery

3. However, based on the consulted experts' clinical experience, IVIg may be considered in fulminant myocarditis or in acute heart failure when an endomyocardial biopsy reveals the presence of a significant lymphocytic infiltrate. Consultation with a cardiologist is necessary in order to assess the appropriateness of prescribing IVIg therapy.
4. Little or no data are available in the literature on the efficacy of Ig for this indication. Based on the clinical experience of the advisory committee's members, IVIg may be considered in the event of failure, contraindication or intolerance to the other therapeutic options in patients with a severe form of the disease.

INSUFFICIENT DATA

INDICATIONS
▸ Pediatric necrotizing fasciitis[5]
▸ Neonatal enterovirus sepsis[6]
▸ Multisystem inflammatory syndrome in adults temporally associated with COVID-19[7]

5. Based on the consulted experts' clinical experience, IVIg may be considered in children with a severe infection.
6. Based on the limited data available in the literature and on the consulted experts' clinical experience, IVIg may be considered for the treatment of severe forms of neonatal enterovirus sepsis.
7. Little or no data are available in the literature on the efficacy of Ig in treating adults with multisystem inflammatory syndrome temporally associated with COVID-19. Based on the consulted experts' clinical experience, IVIg could be considered for this indication.

DOSE AND FREQUENCY OF ADMINISTRATION OF IVIg

- The dose calculator should be used for calculating doses in adults who are overweight or clinically obese, but it can also be used safely in people over 1.52 m (5 feet) and whose weight is not less than their ideal weight. The calculator should not be used for pregnant women.

IVIg	ADULTS AND CHILDREN	
Treatment cycle	Adult: 2 g/kg (total dose) divided over 2 to 5 days Child: 2 g/kg (total dose) divided over 2 days Newborn: 2 g/kg as a single dose[8]	The dose can be adjusted or repeated based on the individual clinical response.

8. If hemodynamic non-tolerance is anticipated, the single IVIg dose can be divided in two, i.e., 1 g/kg for 2 days.

TRANSFUSION REACTIONS ASSOCIATED WITH IVIg

NON-SERIOUS TRANSFUSION REACTIONS (the most common)	SERIOUS TRANSFUSION REACTIONS (usually rare)
▸ Post-IVIg headache, non-hemolytic febrile reaction, chills, urticaria, asthenia, nausea, vomiting, flu-like symptoms, atypical pain, and post-transfusion hypertension or hypotension (list not exhaustive)	▸ Immediate anaphylactic reaction, thromboembolic event, immediate or delayed hemolytic reaction, aseptic meningitis, transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), and acute renal failure (list not exhaustive)

- Serious and non-serious transfusion reactions (particularly those that result in a change in the dose, frequency or type of IVIg administered or that warrant discontinuing the therapy) must be reported to the blood bank using Form AH-520.

RELATIVE CONTRAINDICATIONS AND MAIN PRECAUTIONS CONCERNING IVIg

RELATIVE CONTRAINDICATIONS

- A known allergy to any of the product's ingredients
- A history of severe allergic reaction to Ig (immediate anaphylactic or delayed)

PRECAUTIONS

Hemolysis	Thrombosis	Renal Function
▸ IVIg-related hemolysis is more common in patients with type A, B or AB blood who receive a high total IVIg dose (≥ 2 g/kg). ▸ Monitor the patient for signs and symptoms of hemolysis. If any appear, order the appropriate laboratory tests.	▸ Thrombus formation can occur with any type of Ig in patients with or without risk factors, regardless of the dose administered or the route of administration.	▸ Check renal function if there is an increased risk of acute renal failure. ▸ If renal function deteriorates, consider discontinuing the IVIg.

This guide was developed in collaboration with an expert committee, and INESSS supports the recommendations made.

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