INESSS
LE SAVOIR PREND FORME

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INTRAVENOUS IMMUNOGLOBULIN (IVIg)

USE IN SOLID ORGAN TRANSPLANTATION

This optimal use guide is intended for medical specialists who treat patients who have received a solid organ transplant 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 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 medical specialist.

RECOMMENDATIONS FOR USING IVIG BY INDICATION

A total of 18 solid organ transplantation indications were evaluated – list not exhaustive

IVIg A POSSIBLE TREATMENT OPTION

INDICATIONS	CONDITIONS OF USE
Prevention of transplant rejection in a kidney, heart, lung, pancreas or small intestine transplant recipient	▸ In the presence of hyperimmunization ▸ In the case of HLA- or ABO-incompatible transplantation
Prevention of transplant rejection in a liver transplant recipient	▸ In the case of HLA- or ABO-incompatible transplantation
Treatment of transplant rejection in a solid organ transplant recipient	▸ In the presence of acute humoral transplant rejection
Treatment of a parvovirus B19[1] infection in a solid organ transplant recipient	▸ In the presence of a parvovirus B19 infection
Treatment of a polyomavirus BK infection in a solid organ transplant recipient	▸ In the presence of confirmed polyomavirus BK nephropathy ▸ Especially if concurrent transplant rejection is suspected in a kidney transplant recipient.

1. Based on the clinical experience of the advisory committee's members, IVIg may be considered in case of failure, contraindication or intolerance to the other therapeutic options, to treat parvovirus B19-induced red cell aplasia.

IVIg NOT RECOMMENDED

INDICATIONS	
▸ Prevention of the following infections in a solid organ transplant recipient: • Epstein-Barr virus • Norovirus • HHV-6 • Parvovirus B19 • Polyomavirus BK • Adenovirus • West Nile virus	▸ Treatment of the following infections in a solid organ transplant recipient: • Epstein-Barr virus • Norovirus • HHV-6

HHV-6: human herpesvirus type 6

INSUFFICIENT DATA

INDICATIONS

- Prevention of transplant rejection in a hyperimmunized individual who has received a liver transplant
- Prevention of a respiratory syncytial virus infection in a solid organ transplant recipient
- Treatment of chronic humoral transplant rejection in a solid organ transplant recipient
- Treatment of an infection2 in a solid organ transplant recipient by:
  - The respiratory syncytial virus
  - An adenovirus
  - The West Nile virus

2. In the case of secondary hypogammaglobulinemia, please refer to the optimal use guide on immunoglobulins in clinical immunology.

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: 1 to 2 g/kg (total dose)3 divided over 1 to 5 days[3]	The dose can be adjusted or repeated based on the individual clinical response.

3. IVIg prescribed at a dose greater than 1 g/kg should be administered over several days at a dose not exceeding 1 g/kg/day.

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)

PRÉCAUTIONS

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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