

# CANADIAN IMMUNIZATION GUIDE

## PART 5 – PASSIVE IMMUNIZING AGENTS

PROTECTING CANADIANS FROM ILLNESS



Public Health  
Agency of Canada

Agence de la santé  
publique du Canada

Canada

**TO PROMOTE AND PROTECT THE HEALTH OF CANADIANS THROUGH LEADERSHIP, PARTNERSHIP,  
INNOVATION AND ACTION IN PUBLIC HEALTH.**  
—Public Health Agency of Canada

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## PART 5

## PASSIVE IMMUNIZING AGENTS

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Passive immunizing agents are preparations containing pre-formed antibodies derived from humans or animals, or produced by recombinant DNA technology (refer to [Table 1](#)). Administration of passive immunizing agents can prevent certain infections or reduce the severity of illness caused by the infectious agent.

This chapter describes the types and uses of passive immunizing agents and discusses product administration and storage requirements. The safety profile of standard immune globulin, including common adverse events, is presented.

Several changes have been made to the chapter since the publication of the 2006 Canadian Immunization Guide. Information on the indications and use of the cytomegalovirus immune globulin and the vaccinia immune globulin has been added. The chapter has also been expanded to include information about administration and storage of human immune globulin products. Finally, all recommendations have been updated following the release of Part 4 chapters containing comprehensive information on the use of specific immunizing agents available in Canada.

## PASSIVE IMMUNIZING AGENTS

Passive immunization should be considered when vaccines for active immunization are unavailable or contraindicated, or in certain instances when unimmunized individuals have been exposed to the infective agent and require immediate protection. Passive immunization may also have a role in the management of immunocompromised people unable to adequately respond to a vaccine. The duration of the beneficial effects provided by passive immunizing agents is relatively short-lived and protection may be incomplete.

There are two types of antibody preparations available:

- **Standard immune globulin (Ig) of human origin** – sometimes referred to as “immune serum globulin”, “serum immune globulin” or “gamma globulin”
- **Specific immune globulins of human or animal origin, or produced by recombinant DNA technology** - containing high titres of specific antibodies against a particular microorganism or its toxin. Products of human origin are preferred over those of animal origin because of the high incidence of adverse reactions to animal sera and the longer lasting protection conferred by human immune globulins.

**Table 1: Passive immunizing agents – origin of antibodies**

Passive immunizing agent	Origin of antibodies
<b>Standard immune globulin</b>	
Standard human Ig	Human plasma
<b>Specific immune globulins</b>	
Botulism antitoxin	Horse serum (equine)
Botulism Ig	Human plasma
Cytomegalovirus Ig	Human plasma
Diphtheria antitoxin	Horse serum (equine)
Hepatitis B Ig	Human plasma
Rabies Ig	Human plasma
Respiratory syncytial virus monoclonal antibody (palivizumab)	Recombinant DNA technology
Tetanus Ig	Human plasma
Vaccinia Ig	Human plasma
Varicella zoster Ig	Human plasma

For complete prescribing information, consult the product leaflet or information contained within the product monographs available through Health Canada’s [Drug Product Database](http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php). (<http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php>) Refer to [Contents of Immunizing Agents Available for Use in Canada](#) in Part 1 for a list of passive immunizing agents available for use in Canada and their contents.

## STANDARD IMMUNE GLOBULIN (HUMAN)

Standard human immune globulin (GamaSTAN<sup>®</sup> S/D) is a sterile, concentrated solution for intramuscular (IM) injection containing 15% to 18% immune globulin. It is obtained from pooled human plasma from screened donors and contains mainly IgG with small amounts of IgA and IgM. The potency of each lot of immune globulin product is tested against international standards or reference preparations for at least two different antibodies, one viral and one bacterial. Specific measles and hepatitis A antibody content in standard human immune globulin is not regulated by Health Canada. Theoretically, the concentrations of specific measles and hepatitis A antibody in standard human immune globulin may be insufficient due to lower levels of antibody in the general population as a result of decreased rates of natural infection. This issue is under NACI review. Maximum plasma levels are reached approximately 2 days after IM injection, and the half-life in the circulation of individuals with normal IgG levels is 23 days.

Subcutaneous (Sc) and intravenous (IV) immune globulin (IVIg) are used for continuous passive immunization for persons with selected congenital or acquired immunoglobulin deficiency states and as an immunomodulator in certain diseases. Discussion of uses of these products is beyond the scope of the *Canadian Immunization Guide*. Consult appropriate resources such as the manufacturer's product leaflet or the product monographs.

### RECOMMENDATIONS FOR USE

Prophylactic use of IM Ig has been shown to be effective in a limited number of clinical situations, including exposure to measles and hepatitis A. The dose varies by indication, and recommendations in the product leaflet or product monograph should be followed.

#### Measles

Prophylactic use of Ig has been shown to be effective in modifying or preventing disease if administered within 6 days after exposure to measles, however, it should be given as soon as possible after exposure when indicated. Ig should be considered for susceptible pregnant women and susceptible immunocompromised contacts of measles, and for children less than 6 months of age; measles-containing vaccine is contraindicated in the two former groups and effectiveness and safety has not been established in the latter group. Ig should also be considered for susceptible immunocompetent contacts of measles who are 6 months of age and older and who present more than 72 hours after exposure (when MMR vaccine no longer provides post-exposure protection) but within 6 days after exposure (when Ig may still provide post-exposure protection).

The recommended dose of Ig for healthy individuals exposed to measles is 0.25 mL/kg of body weight given by the IM route. The dose for exposed individuals who are immunocompromised is 0.5 mL/kg of body weight. A maximum dose of 15 mL should not be exceeded.

Individuals receiving replacement IVIg (400 mg/kg of body weight or higher) are considered protected and do not require Ig if the last dose of IVIg was received within the three weeks prior to measles exposure.

Unless it is contraindicated, individuals who receive Ig for the prevention of measles should receive measles-containing vaccine after specified intervals, once the measles antibodies administered passively have degraded. Refer to [Blood products, human immune globulin and timing of immunization](#) in Part 1 for additional information.

Refer to [Measles Vaccine](#) in Part 4 for additional information.

## Hepatitis A

### Pre-exposure prophylaxis

Hepatitis A (HA) vaccine is the preferred agent for pre-exposure prophylaxis. Ig will provide protection against HA when administered IM before exposure. Ig is indicated for pre-exposure prophylaxis for:

- infants less than one year of age
- persons with a history of anaphylaxis after previous administration of the HA vaccine and those with proven immediate or anaphylactic hypersensitivity to any component of the HA vaccine or its container
- immunocompromised persons. Immunocompromised people should receive Ig in addition to HA vaccine because they may not respond fully to the vaccine.

Administering Ig immediately before travel will ensure that protective concentrations of antibody are adequate for short-term (up to 6 months) travel.

The recommended dose of Ig varies according to the duration of required protection. In general, for protection lasting less than 3 months the dose is 0.02 mL/kg of body weight. If protection is required for 3 months or longer, 0.06 mL/kg of body weight should be administered and repeated every 6 months.

### Post-exposure prophylaxis

Hepatitis A (HA) vaccine is the preferred agent for post-exposure prophylaxis. Ig is the recommended post-exposure immunoprophylactic agent:

- for infants less than one year of age
- for persons with a history of anaphylaxis after previous administration of the HA vaccine and those with proven immediate or anaphylactic hypersensitivity to any component of the HA vaccine or its container
- if HA vaccine is unavailable
- for immunocompromised persons. Immunocompromised people should receive Ig in addition to HA vaccine because they may not respond fully to the vaccine.

For post-exposure prophylaxis, the dose of Ig is usually 0.02 mL/kg of body weight, given as soon as possible after an exposure. Efficacy of Ig is unknown if more than 14 days have elapsed since the last exposure.

Refer to [Hepatitis A Vaccine](#) in Part 4 for more information about HA vaccine.

## Rubella

Passive immunization with Ig is not effective in preventing rubella. Ig given soon after exposure to rubella may modify or suppress symptoms but may not prevent infection, including congenital infection. Therefore, the routine use of Ig in susceptible women exposed to rubella early in pregnancy is not recommended.

## SPECIFIC IMMUNE GLOBULINS

Specific immune globulins are derived from the pooled sera of people with antibodies to specific infectious agents; antisera from animals (usually horses that are hyper-immunized against a specific organism) when human products are not available; or recombinant DNA technology. Immune globulins from human or animal sources are made by more than one B cell clone (polyclonal) and can bind to heterogeneous antigens. Antibodies produced through recombinant DNA technology originate from a single clone of B



cells (monoclonal) and are specific to only one antigen. A monoclonal antibody product is available for the prevention of respiratory syncytial virus (RSV) infection. Because of the relatively high risk of a specific type of immunological reaction (known as serum sickness) following the use of animal products, human Ig should be used whenever possible.

Some specific Ig products are only available on an emergency basis and require application to [Health Canada's Special Access Programme \(SAP\)](http://www.hc-sc.gc.ca/dhp-mps/acces/index-eng.php). (<http://www.hc-sc.gc.ca/dhp-mps/acces/index-eng.php>) The SAP provides access to non-marketed drugs for health care providers treating people with serious or life-threatening conditions when conventional therapies have failed, are unsuitable, or unavailable. The SAP authorizes a manufacturer to sell a product that cannot otherwise be sold or distributed in Canada based on the submitted *Special Access Request Form* which can be obtained from the [SAP website](http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-drogués/index-eng.php) (<http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-drogués/index-eng.php>) or by contacting the SAP office (telephone: 613-941-2108; fax: 613- 941-3194 - available 24 hours a day, 7 days a week). The health care provider should be prepared to provide the information required on the *Special Access Request Form* to the SAP on-call officer. Public health should be contacted for assistance in obtaining specific Ig products.

### **BOTULISM ANTITOXIN (BATx, EQUINE) AND BOTULISM IMMUNE GLOBULIN (BIG-IV, HUMAN)**

Botulism antitoxin or botulism immune globulin is used therapeutically in people with established or suspected botulism as well as prophylactically in asymptomatic people strongly suspected of having eaten food contaminated with the botulism toxin. Health Canada's [Botulism-Guide for Health Care Professionals](http://www.hc-sc.gc.ca/fn-an/legislation/guide-ld/botulism-botulisme-prof-eng.php) provides information about botulism including clinical specimen collection and submission. (<http://www.hc-sc.gc.ca/fn-an/legislation/guide-ld/botulism-botulisme-prof-eng.php>) Botulism antitoxin and botulism immune globulin are not authorized for sale in Canada and are currently only available through the SAP. Only the following four products can be accessed through the SAP:

1. Novartis trivalent Types ABE
2. NP-018 (heptavalent) Types A to G
3. BabyBIG<sup>®</sup>, Botulism Immune Globulin Intravenous; accessed from the Infant Botulism Treatment and Prevention Program at the California Department of Public Health
4. Botulism antitoxin Type AB and Type E; accessed from the Butantan Institute in Brazil

BabyBIG<sup>®</sup> is a human-derived botulism antitoxin indicated in the treatment of infant botulism for infants up to one year of age. The manufacturers of BabyBIG<sup>®</sup> do not permit pre-orders of this product and it can only be obtained by directly contacting the SAP. For additional information on BabyBIG<sup>®</sup>, health care providers can contact the California Department of Public Health, [Infant Botulism Treatment and Prevention Program](http://infantbotulism.org/) at 510-231-7600. (<http://infantbotulism.org/>)

Health care providers should request botulism antitoxin through their local public health officials. Public health officials will provide the botulism antitoxin from the Provincial/Territorial antitoxin stockpile or request it through the Public Health Agency of Canada's (PHAC) [National Emergency Stockpile System](http://www.phac-aspc.gc.ca/ep-mu/ness-eng.php) or SAP. (<http://www.phac-aspc.gc.ca/ep-mu/ness-eng.php>)

Testing for hypersensitivity to the equine antitoxin preparations should be carried out in accordance with the manufacturer's recommendations before the antitoxin is administered. If sensitivity tests are positive, desensitization must be undertaken according to the manufacturer's recommendations.

### **CYTOMEGALOVIRUS IMMUNE GLOBULIN (CMVlg)**

Cytomegalovirus immune globulin (Cytogam<sup>®</sup>) is a solution of cytomegalovirus (CMV) Ig for IV administration. It is prepared from pooled human plasma from screened donors and contains relatively high levels of antibody against CMV. CMVlg can be used for:

- reduction of the risk of primary CMV disease in CMV seronegative transplant recipients
- adjunctive therapy for CMV pneumonitis in transplant recipients

The maximum recommended dose per infusion is 150 mg/kg of body weight. Since CMVlg is indicated in specific circumstances only, it should be used in consultation with a specialist in immunodeficiency. Further discussion of CMVlg is beyond the scope of the *Canadian Immunization Guide*.

### **DIPHTHERIA ANTITOXIN (DATx, EQUINE)**

Anti-diphtheria serum is a specific immune globulin preparation for IM or IV administration, obtained from the plasma of horses hyper-immunized with diphtheria toxoid. The antitoxin is available on an emergency basis through local public health officials.

Diphtheria antitoxin should be administered when there is clinical suspicion of diphtheria. Bacteriologic confirmation is not required to initiate treatment. Testing for hypersensitivity to the preparation should be carried out before diphtheria antitoxin is administered. If sensitivity tests are positive, desensitization must be undertaken according to the manufacturer's recommendations. The method of testing for sensitivity to equine serum, as well as the dose and route of administration, are described in the manufacturer's product leaflet.

Diphtheria antitoxin is not recommended for prophylaxis of close contacts of diphtheria cases, whether immunized or not, given the substantial risk of allergic reaction to equine serum and lack of evidence of additional benefit of antitoxin for contacts who have received antimicrobial prophylaxis.

Refer to [Diphtheria Toxoid](#) in Part 4 for additional information.

### **HEPATITIS B IMMUNE GLOBULIN (HBIG)**

Hepatitis B immune globulin preparations (HyperHEP B™ S/D, HepaGam B™) are solutions of hepatitis B Ig for IM administration, prepared from pooled human plasma from screened donors with a high level of antibody to hepatitis B surface antigen. HBIG provides immediate short-term passive immunity.

For post-exposure prophylaxis, hepatitis B (HB) vaccine is the most important intervention, providing 90% of the protection from hepatitis B; HBIG may provide additional protection and should be offered to susceptible individuals (refer to [Table 2](#)). HBIG may be given at the same time as HB vaccine but at different injection sites, using separate needles and syringes. HBIG administered concurrently with vaccine does not interfere with the antibody response to the vaccine. The timing and use of HBIG is currently under review by the National Advisory Committee on Immunization (NACI).



**Table 2: Hepatitis B post-exposure prophylaxis, recommendations for use of HBIg**

Post-exposure prophylaxis circumstance	Recommendations
Infant born to a mother with acute or chronic hepatitis B infection	<ul style="list-style-type: none"> <li>All infants born to infected mothers should be given an IM dose of 0.5 mL HBIg as soon as possible after birth (preferably within 12 hours) in addition to the first of a three dose series of HB vaccine (premature infants weighing less than 2,000 grams at birth require four doses of vaccine). The efficacy of HBIg decreases significantly after 48 hours, but HBIg may be given up to 7 days after birth.</li> </ul>
Percutaneous or mucosal exposure to blood or body fluids potentially containing hepatitis B virus	<ul style="list-style-type: none"> <li>HBIg should be given to susceptible individuals (based on their immunization and antibody status, and the infectious status, if known, of the source) within 48 hours after exposure<sup>1</sup>. Efficacy of HBIg decreases significantly after 48 hours, but HBIg may be given up to 7 days after exposure.</li> <li>Dose of HBIg for older infants, children and adults is 0.06 mL/kg of body weight IM.</li> </ul>
Sexual contacts of an acute case or chronic carrier of hepatitis B	<ul style="list-style-type: none"> <li>A single<sup>1</sup> IM dose of HBIg (0.06 mL/kg of body weight) should be given within 48 hours after exposure.</li> <li>Efficacy of HBIg decreases significantly after 48 hours, but may be given up to 14 days from the last sexual contact.</li> </ul>

<sup>1</sup> If known HB vaccine non-responder, or if HB vaccine contraindicated, give second dose of HBIg 4 weeks after the first dose

Refer to [Hepatitis B Vaccine](#) in Part 4 for additional information.

### **RABIES IMMUNE GLOBULIN (RaBIg)**

Rabies immune globulin products (IMOGAM® Rabies Pasteurized, HYPERRAB® S/D) are solutions of anti-rabies Ig for IM administration, prepared from the pooled human plasma of screened donors immunized with rabies vaccine. RaBIg is available on an emergency basis through local public health officials.

Post-exposure rabies prophylaxis of previously unimmunized individuals consists of both RaBIg and rabies vaccine. RaBIg provides immediate passive protection that persists for a short period of time (half-life of about 21 days) until the exposed person mounts an immune response to the rabies vaccine.

The recommended dose of RaBIg is 20 IU/kg of body weight for all age groups given on the first day of initiation of therapy. Because of possible interference of RaBIg with the immune response to the rabies vaccine, the dose of RaBIg should not be exceeded. If possible, the full dose of RaBIg should be thoroughly infiltrated into the wound and surrounding area. Any remaining volume of RaBIg should be injected, using a different needle, intramuscularly at a site distant from the site of vaccine administration. When more than one wound exists, each wound should be locally infiltrated with a portion of the RaBIg using a separate needle. In such instances, the RaBIg can be diluted two-fold to three-fold in a solution of 0.9% sodium chloride in order to provide the full amount of RaBIg required for thorough infiltration of all wounds. If the site of the wound is unknown, the entire dose should be administered intramuscularly at a separate site from where the rabies vaccine is administered.

Rabies vaccine and Rablg may be given at the same time but at different injection sites, using separate needles and syringes. Rabies vaccine and Rablg should never be mixed in the same syringe. If Rablg is not administered as recommended at the initiation of the rabies vaccine series, Rablg can be administered up to day 7 after vaccine is initiated.

Refer to [Rabies Vaccine](#) in Part 4 for additional information.

### RESPIRATORY SYNCYTIAL VIRUS (RSV) MONOCLONAL ANTIBODY (RSVAb)

Respiratory syncytial virus monoclonal antibody (SYNAGIS® [palivizumab]) is a humanized monoclonal antibody to RSV produced by recombinant DNA technology and composed of 95% human and 5% murine amino acid sequences. RSVAb is not derived from human Ig, and is free of potential contamination from blood-borne infectious agents.

RSVAb prophylaxis is recommended for children who are at high risk of severe RSV disease as outlined in [Table 3](#).

**Table 3: Recommended recipients of RSVAb for RSV prophylaxis**

Recommended recipients	Comments
<b>Infants born prematurely</b>	
Infants born prematurely at 32 weeks or less gestational age	<ul style="list-style-type: none"> <li>All infants born prematurely at 32 weeks 6 days gestation or earlier and who are 6 months of chronological age or younger at the start of the local RSV season should be given RSV prophylaxis</li> </ul>
Infants born prematurely between 33 and 35 weeks gestational age	<ul style="list-style-type: none"> <li>Selected infants born prematurely between 33 and 35 weeks of gestational age and who are less than 6 months of age at the start of the local RSV season may benefit from the administration of RSVAb.</li> <li>The decision to offer RSVAb to select infants in this birth cohort should be based on local considerations.</li> </ul>
<b>Children with lung disease</b>	
Children younger than 24 months of age with chronic lung disease of prematurity or bronchopulmonary dysplasia	<ul style="list-style-type: none"> <li>Children with chronic lung disease who require oxygen and/or medical therapy (including drug treatment) within the 6 months preceding the start of the local RSV season</li> </ul>
<b>Children with heart disease</b>	
Children younger than 24 months of age with hemodynamically significant cyanotic and acyanotic heart disease	<ul style="list-style-type: none"> <li>In infants receiving prophylaxis with RSVAb, an extra dose of RSVAb should be administered following cardiopulmonary bypass procedures, when the patient is medically stable and if the patient remains at risk of severe disease or complications from RSV infection.</li> <li>Children with hemodynamically insignificant cardiac lesions such as patent ductus arteriosus, or uncomplicated small atrial or ventral septal defects without other risk factors are <i>not recommended</i> to receive RSV prophylaxis.</li> </ul>

Recommended recipients	Comments
<b>Children living in rural and remote communities</b>	
Infants born prematurely between 33 and 35 weeks gestational age who live in rural or remote communities	<ul style="list-style-type: none"> <li>Infants born between 33 and 35 weeks gestational age who are less than 6 months of age at the start of the local RSV season and who live in rural or remote communities may be considered for prophylaxis according to an assessment of access to medical care (e.g., require air transportation to hospital facilities) and other factors known to increase risk.</li> </ul>
Inuit children younger than 6 months of age at start of RSV season	<ul style="list-style-type: none"> <li>Regardless of gestational age, all Inuit children younger than 6 months of age at the onset of the RSV season in northern remote communities should be considered to receive RSV prophylaxis.</li> <li>Other First Nations and Metis children less than 6 months of age (not identified in the above risk groups) – RSV prophylaxis is <i>not recommended</i> due to insufficient data.</li> </ul>

RSVAb is administered by the IM route only; the preferred site of injection is the anterolateral thigh. RSVAb is administered every 4 weeks at a dose of 15 mg/kg of body weight for each of the five months during the period of high risk of exposure to RSV (maximum of 5 doses). Providing the first dose at least 2 weeks prior to the onset of the local RSV season is recommended; for neonates, initial dosing just prior to hospital discharge during the RSV season is recommended.

Children who become infected with RSV while taking RSVAb prophylaxis should continue to receive their scheduled monthly doses of RSVAb throughout the RSV season, because RSV infection itself does not confer protective immunity.

### TETANUS IMMUNE GLOBULIN (Tlg)

Tetanus immune globulin (HYPERTET™ S/D) is a solution of tetanus Ig for IM administration prepared from pooled human plasma of screened donors immunized with tetanus toxoid. Tlg provides immediate passive protection until the exposed person mounts an immune response to the tetanus toxoid.

Individuals who are previously unimmunized or incompletely immunized (unknown or less than 3 doses of tetanus-toxoid containing vaccine) and sustain a wound that is other than minor and clean should receive both Tlg and tetanus toxoid-containing vaccine (as appropriate for age and immunization history) given at different injection sites using separate needles and syringes. Indications for post-exposure prophylaxis are outlined in [Table 4](#).

**Table 4: Guide to tetanus prophylaxis in wound management**

History of tetanus immunization	Clean, minor wounds		All other wounds	
	Tetanus toxoid-containing vaccine <sup>1</sup>	Tlg	Tetanus toxoid-containing vaccine <sup>1</sup>	Tlg <sup>2</sup>
Unknown or less than 3 doses in a vaccine series <sup>3</sup>	Yes	No	Yes	Yes
3 or more doses in a vaccine series and <b>less than 5 years</b> since last booster dose	No	No	No	No <sup>4</sup>
3 or more doses in a vaccine series and <b>more than 5 years but less than 10 years</b> since last booster dose	No	No	Yes	No <sup>4</sup>
3 or more doses in a vaccine series and <b>more than 10 years</b> since last booster dose	Yes	No	Yes	No <sup>4</sup>

<sup>1</sup> Refer to [Tetanus Toxoid](#) in Part 4 for specific tetanus toxoid-containing vaccine recommendation based on age.

<sup>2</sup> Given at different injection sites using separate needles and syringes.

<sup>3</sup> Refer to [Tetanus Toxoid](#) in Part 4 for information about vaccine series.

<sup>4</sup> Yes, if known to have a humoral immune deficiency state.

Tlg = tetanus immune globulin

Some individuals with humoral immune deficiency (e.g., HIV, agammaglobulinemia or hypogammaglobulinemia) may not respond adequately to tetanus toxoid-containing vaccine. Individuals with humoral immune deficiency who have wounds that are not minor and clean should receive both Tlg and tetanus toxoid-containing vaccine, regardless of the time elapsed since the last booster.

The recommended dose of Tlg for adults and children is 250 units by IM injection. It is advisable to administer the entire contents of the vial of Tlg regardless of the child's size; theoretically the same amount of toxin will be produced in a child or adult's body by the infecting tetanus organism.

Refer to [Tetanus Toxoid](#) in Part 4 for additional information.

### VACCINIA IMMUNE GLOBULIN (VIG)

Vaccinia immune globulin intravenous is a solution of gamma globulin from the serum of individuals recently immunized with smallpox vaccine. It is indicated to treat severe smallpox vaccine-associated adverse events: eczema vaccinatum, progressive vaccinia, severe or recurrent generalized vaccinia, and extensive lesions resulting from accidental implantation (transfer of vaccinia virus from the primary vaccination site to other parts of the body). VIG is ineffective in the treatment of post-vaccinal encephalitis and has no role in the treatment of smallpox.

The PHAC [Centre for Emergency Preparedness and Response](http://www.phac-aspc.gc.ca/cepr-cmiu/) (<http://www.phac-aspc.gc.ca/cepr-cmiu/>) has a supply of VIG based on a requirement of 1 dose of VIG for every 10,000 doses of smallpox vaccine. The Canadian Smallpox Contingency Plan indicates that VIG would be sent to the provinces/territories at the same time as smallpox vaccine and related supplies if smallpox occurs in Canada. Refer to [Smallpox Vaccine](#) in Part 4 for additional information.

### VARICELLA ZOSTER IMMUNE GLOBULIN (VarIg)

Varicella zoster immune globulin (VariZIG™) is a freeze-dried preparation of varicella zoster Ig prepared from the pooled human plasma of screened donors with high titres of antibodies to varicella zoster virus.

Varlg is recommended for the prevention or reduction in severity of infection within 4 days (96 hours) of the most recent exposure to the varicella zoster virus. The decision to administer Varlg should be based on fulfilling **all** of the following four criteria:

1. The *exposed person is susceptible* to varicella (except for recipients of HSCT).
2. There has been a *significant exposure* to a person with varicella or herpes zoster (HZ). The following situations are significant exposures to varicella zoster virus:
  - continuous household contact (living in the same dwelling) with a person with varicella or being indoors for more than 1 hour with a case of varicella
  - being in the same hospital room for more than 1 hour, or more than 15 minutes of face-to-face contact with a person with varicella
  - touching the lesions of a person with active varicella
  - close contact with a person with HZ. Close contact with HZ includes:
    - touching the rash, exposed lesion or vesicle fluid
    - contact with an individual who has disseminated HZ
    - contact with articles freshly soiled by discharges from vesicles
    - contact with articles freshly soiled by mucous membrane secretions of a person with disseminated HZ
    - exposure to an immunocompromised person with localized HZ anywhere on the body as their viral shedding may be greater.
3. The *exposed person is at increased risk of severe varicella* including:
  - pregnant women
  - **newborn infants of mothers who develop varicella** during the 5 days before to 48 hours after delivery
  - selected neonates in intensive care settings
  - **immunocompromised persons (including those with HIV with CD4 cell count < 200 x 106/L or CD4 percentage < 15%)**
  - **recipients of HSCT regardless of pre-transplant varicella immune status**, history of varicella disease or vaccination, or positive serologic test results
4. *Post-exposure immunization with univalent varicella vaccine is contraindicated.*

Varlg may be used within 96 hours from the most recent exposure. Protection conferred by Varlg lasts approximately 3 weeks. Subsequent exposures occurring more than 3 weeks after a dose of Varlg require additional doses of Varlg if the criteria for administration, as specified above, are met.

The recommended dose of Varlg is 125 IU/10 kg of body weight up to a maximum of 625 IU. The minimum dose is 125 IU. Varlg should be given by the IM route.

Individuals receiving replacement IVIg (400 mg/kg of body weight or higher) are considered protected and do not require Varlg if the last dose of IVIg was received within the three weeks prior to varicella exposure.

Refer to [Varicella Vaccine](#) in Part 4 for additional information.

## HUMAN IMMUNE GLOBULIN ADMINISTRATION AND STORAGE

Large volumes of immune globulin for IM injection (greater than 2 mL for children or greater than 3-5 mL for adults, depending on muscle mass) should be divided and injected at two or more sites. Currently available human Ig preparations, with the exception of IVIg, Varlg, CMVIg, VIG, and BIG-IG, must not be given IV because of the risk of rare anaphylactic reactions.

Human Ig preparations should be stored at +2°C to +8°C. Do not freeze.



## HUMAN IMMUNE GLOBULIN SAFETY AND ADVERSE EVENTS

Human Ig preparations are among the safest blood-derived products available. Plasma donors undergo a comprehensive screening process prior to donation and individuals with known risks for blood-borne pathogens are excluded from donating plasma for Ig preparations. Donated plasma is tested (at a minimum) for HIV, hepatitis B, hepatitis C and other infectious agents, and, if positive, is not used for the manufacturing of Ig products. In addition, donated plasma undergoes multiple purification procedures for human virus inactivation or removal during preparation of Ig products.

For safety information about products prepared from animal serum, consult the product leaflet. For safety information about specific Ig products consult the product leaflet or information contained within the product monographs available through Health Canada's [Drug Product Database](http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php). (<http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php>)

### COMMON AND LOCAL ADVERSE EVENTS

Injection site reactions following receipt of standard human Ig include tenderness, erythema and stiffness of local muscles, which may persist for several hours. Mild fever or malaise may occasionally occur.

### LESS COMMON AND SERIOUS OR SEVERE ADVERSE EVENTS

Less common side effects following receipt of standard human Ig include flushing, headache, chills and nausea. Urticaria, angioedema and anaphylactic reactions may occur rarely.

### GUIDANCE ON REPORTING ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

Health care providers are asked to report, through local public health officials, any serious or unexpected adverse event felt to be temporally related to immunization with a passive immunizing agent. An unexpected AEFI is an event that is not listed in available product information but may be due to the immunization, or a change in the frequency of a known AEFI. Refer to [Vaccine Safety](#) in Part 2 and [Reporting Adverse Events Following Immunization \(AEFI\) in Canada](#) for additional information about AEFI reporting. ([http://webqa.phac-aspc.gc.ca/im/ae-fi-essi\\_guide/index-eng.php](http://webqa.phac-aspc.gc.ca/im/ae-fi-essi_guide/index-eng.php))

### CONTRAINDICATIONS AND PRECAUTIONS

HBIg, VarIg and standard human Ig preparations are contraindicated in persons with history of anaphylaxis after previous administration of the product and in persons with proven immediate or anaphylactic hypersensitivity to any component of the product or its container. Refer to [Contents of Immunizing Agents Available for Use in Canada](#) in Part 1 for a list of passive immunizing agents available for use in Canada and their contents. If indicated, TIg and RabIg should be given with caution to persons with a history of prior systemic allergic reactions following the administration of human Ig preparations.

In situations of suspected hypersensitivity or non-anaphylactic allergy to product components, investigation that may involve administration in a controlled setting is indicated. Consultation with an allergist is advised.

Human Ig preparations should not be given to people with known isolated IgA deficiency unless the benefit outweighs the risk, in which case the product should be given with caution and under close observation.

For people with bleeding disorders, special measures need to be considered before administering IM injections. Any bleeding disorder should be optimally controlled. For example, hemophiliacs may receive clotting factor concentrates to optimize their clotting factor level. There is some evidence to suggest that IM administration may generally be safe when given with a small gauge needle (23 gauge or smaller) and firm pressure is applied to the injection site for 5-10 minutes.



## DRUG INTERACTIONS

Passive immunization with human Ig preparations can interfere with the immune response to MMR, measles-mumps-rubella-varicella (MMRV) and univalent varicella vaccines. These vaccines should be given at least 14 days prior to administration of a human Ig preparation, or delayed until the antibodies in the Ig preparation have degraded. Refer to [Blood Products, Human Immune Globulin and Timing of Immunization](#) in Part 1 for additional information.

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