Pocket Guide for Immunizers:

Pooled Polyclonal Immunoglobulin Products

The purpose of this pocket guide is to serve as a tool for health care providers to learn more about immunoglobulin products that provide passive immunization, enabling them to support the use and administration of these products to their patients when indicated.

Immunoglobulin products are a form of passive immunization. They provide instant, ready-formed antibodies that are needed for rapid protection against some vaccine-preventable diseases.

Vaccination stimulates and trains the body's immune system to produce antibodies on its own, providing more long-term immunity that develops over time. Passive immunity involves conferring immunity to someone via pre-formed antibodies, instead of having their immune system produce their own antibodies.

Most immunoglobulins used in a public health context are for the rapid and urgent protection of people who are susceptible – generally those who have not been previously vaccinated – after an exposure to a vaccine-preventable disease (i.e., post-exposure prophylaxis, or PEP). Immunoglobulin products provide short-term protection and are not a replacement for vaccines, since the latter offer long-term protection. However, in situations where vaccination has not been previously received and exposure to a vaccine-preventable disease requires rapid protection, immunoglobulin products become an important part of the healthcare provider's toolkit.

This pocket guide references recommendations made in the *Canadian Immunization Guide* Chapters on *Hepatitis B Vaccines*, *Rabies Vaccines*, *Tetanus Toxoid*, *Varicella (Chickenpox) Vaccines*, *Measles Vaccines*, *Hepatitis A Vaccines*, and *Blood Products, Human Immunoglobulin and Timing of Immunization* from the Public Health Agency of Canada and commentary made by expert reviewers. Supplementary documents referenced in this guide include: *Basic immunology and vaccinology: Canadian Immunization Guide*, *Contents of immunizing agents authorized for use in Canada: Canadian Immunization Guide*, *Immunoglobulin products*: Canadian Blood Services, *Updated NACI recommendation for measles post-exposure prophylaxis*, and *Canadian Immunization Guide: Vaccine administration practices*.

Pocket Guide for Immunizers:

Pooled Polyclonal Immunoglobulin Products

Table of Contents

Pocket Guide for Immunizers:

Pooled Polyclonal Immunoglobulin Products

What immunoglobulin products are available?

The immunoglobulin products discussed in this pocket guide are blood products derived from the pooled human plasma of screened blood donors. There are two types of products discussed in this pocket guide:

- Immunoglobulin products containing antibodies against specific diseases from donors with high antibody titres for the vaccine-preventable disease (e.g., varicella and hepatitis B) or donors vaccinated against the disease (e.g., tetanus and rabies).
- Human immunoglobulin pooled from general donors, used for post-exposure prophylaxis of measles and hepatitis A.

All donors of immunoglobulin products are screened for bloodborne infections, and the products undergo rigorous processes to remove potential infections and minimize the risk of bloodborne diseases, thus contributing to their safety.

See Table 1 for a list of approved immunoglobulin products in Canada that are typically used in a public health context, and the infectious diseases they provide antibodies against.

Note that several specific immunoglobulin products are available only on an emergency basis from local public health units. In some cases, Canadian Blood Services (contact here) or Héma-Québec (contact here) may be involved in obtaining immunoglobulin products for emergency use.

Pocket Guide for Immunizers:

Pooled Polyclonal Immunoglobulin Products

Table 1: Preparations of immunoglobulin products authorized for use in Canada that are commonly used in a public health context

Class of immunoglobulin		Used for	Products Available
Immunoglobulins that protect against specific diseases *Contain high level of antibodies against specific diseases*		Hepatitis B PEP	• HyperHEP B® S/D • HepaGam B®
		Tetanus PEP	• HYPERTET® S/D • HyperTET®
		Rabies PEP	• HyperRAB® • KamRAB™
		Varicella Zoster PEP	• VariZIG®
Human immunoglobulin (Ig) *Contains pooled antibodies from the general population*	Intramuscular human immunoglobulin (IMIg)	Measles PEP[2] Hepatitis A PrEP[3] and PEP	• GamaSTAN®
	Intravenous human immunoglobulin (IVIg)	Measles PEP[2]	• Gammagard® • Gamunex® • IGIVnex • Privigen® • Panzyga®

Abbreviations: PEP = post-exposure prophylaxis; PrEP = pre-exposure prophylaxis; IMIg = human immunoglobulin administered intramuscularly; IVIg = human immunoglobulin administered intravenously

[1] Some immunoglobulin products approved for use in Canada have medical indications aside from those listed in this table. However, listing their uses would be beyond the scope of this pocket guide.

[2] Human immunoglobulin for post-exposure prophylaxis of measles can be given either intramuscularly or intravenously; see the Use of Human Immunoglobulin for Measles section below.

[3] Human immunoglobulin is used in some cases for the prevention of hepatitis A before exposure (pre-exposure prophylaxis), as well as for post-exposure prophylaxis; see the Use of Human Immunoglobulin for Hepatitis A section below.

Recommendations for use of immunoglobulin products in public health

Hepatitis B Immunoglobulin (HBIg)

Active hepatitis B vaccination (pre-exposure) is the most important form of prevention against hepatitis B. Following exposure to hepatitis B, the hepatitis B vaccine is also the most important post-exposure intervention for susceptible individuals, which includes people who have never been immunized against hepatitis B, or who are not fully protected against hepatitis B infection based on their post-vaccination serology results. HBIg may provide additional protection when administered in conjunction with the vaccine, and should thus be offered to:

- newborns of a mother or birthing parent who has acute or chronic hepatitis B infection,
- susceptible individuals with percutaneous (through the skin) or mucosal exposure to an infected or high-risk hepatitis B exposure source, and
- people who have had sexual contact with anyone who has acute or chronic hepatitis B infection.

Guidance on who is considered a high-risk and low-risk hepatitis B exposure source can be found in the *Hepatitis B chapter* of the *Canadian Immunization Guide*. Within the same chapter, Figure 1 (infected or high-risk source) and Figure 2 (uninfected or low-risk source) provide detailed algorithms to guide the post-exposure management of exposed individuals based on their vaccination history and post-vaccination serology results.

For high-risk exposures (hepatitis B-infected or high-risk sources), and known hepatitis B vaccine non-responders (who have previously received 2 full series of the hepatitis B vaccine without achieving a titre of ≥10 IU/L), a second dose of HBIg should be given 4 weeks after the initial HBIg dose.

HBIg may be given at the same time as hepatitis B vaccine without interference, but a separate needle, syringe, and anatomical injection site must be used.

Table 2 provides general guidance on when to administer HBIg and/or the hepatitis B vaccine to specific susceptible groups exposed to hepatitis B. For additional details, please see the *Hepatitis B Vaccines chapter* of the *Canadian Immunization Guide*.

Table 2: Recommended usage of HBIg and hepatitis B vaccine for hepatitis B post-exposure prophylaxis

Exposed group	HBIg recommendation	Hepatitis B vaccine recommendation
All infants whose birthing mother or birthing parent is infected with hepatitis B	• One dose of HBIg should be administered as soon as possible within 12 hours of birth; can be administered up to 7 days after birth	• A series of hepatitis B vaccine should begin at the same time HBIg is given
Susceptible individuals who have had sexual contact with a person infected with hepatitis B	• One dose of HBIg should be administered within 48 hours of sexual exposure • If more than 48 hours have passed, HBIg may still be administered (with lower efficacy) within 14 days	• Hepatitis B vaccine should be given at the same time HBIg is given
Susceptible individuals who have had percutaneous (through the skin) or mucosal exposure to blood or other bodily fluids potentially containing hepatitis B[1]	• One dose of HBIg should be administered within 48 hours of exposure (or, with lower efficacy, within 7 days)	• A dose of hepatitis B vaccine should be administered, or a course of hepatitis B vaccine should begin, continue, or be completed, depending on the person's immunization status[2]

[1] For hepatitis B-infected or high-risk sources, if the exposed person is a known hepatitis B vaccine non-responder (has previously received 2 full series of the hepatitis B vaccine without achieving a titre of ≥10 IU/L), a second dose of HBIg should be given 4 weeks after the initial HBIg dose.

[2] Please see Figure 1 in the *Hepatitis B Vaccines chapter* of the *Canadian Immunization Guide* to view an algorithm detailing when to administer the hepatitis B vaccine after percutaneous or mucosal exposure to hepatitis B.

HBIg is not recommended as part of a post-exposure regimen for:

- those with an uninfected or low-risk exposure source, OR
- those with a hepatitis B-infected or high-risk exposure source if the exposed person has achieved a titre of ≥10 IU/L after vaccination at any time.

Tetanus Immunoglobulin (TIg)

Routine immunization with tetanus toxoid vaccine is the most important protection against tetanus. Should an unimmunized person or an incompletely immunized person (fewer than 3 doses, or unknown vaccination status) experience a tetanus-prone wound (i.e., anything other than a minor and clean wound), they should be administered a single dose of TIg in conjunction with the tetanus toxoid vaccine (and additional vaccine doses to complete a primary series). TIg will provide immediate protection while the patient's immune response to the vaccine develops. If TIg is administered in conjunction with the tetanus toxoid vaccine, a separate needle, syringe, and anatomical injection site must be used. TIg is also indicated for people with humoral immunodeficiency (for example from HIV, agammaglobulinemia or hypogammaglobulinemia) who experience a tetanus-prone wound, regardless of vaccination history.

Those who have previously completed a course of tetanus toxoid vaccine consisting of 3 or more doses do not need to receive TIg, regardless of the status of their wound. For some individuals, revaccination with tetanus toxoid vaccine may be indicated after sustaining an injury.

TIg should be given as soon as possible, ideally within 24 hours after a tetanus-prone wound has occurred. However, TIg can be given up to 21 days after sustaining injury (based on the incubation period of 3-21 days).

See Table 1 of the *Tetanus Vaccines chapter* of the *Canadian Immunization Guide* for further details.

Pocket Guide for Immunizers:

Pooled Polyclonal Immunoglobulin Products

Rabies Immunoglobulin (RabIg)

Rabies is almost always a fatal disease unless it is prevented with appropriate post-exposure management. Exposure to potentially rabid animals should be managed jointly with your local public health unit. The *Rabies Vaccines chapter* of the *Canadian Immunization Guide* provides details to assist in determining when post-exposure prophylaxis is indicated after an exposure to a potentially rabid animal. Table 2 within the same chapter provides in-depth guidance on post-exposure prophylaxis management by animal type.

If post-exposure prophylaxis is indicated, it should be given as soon as possible. RabIg and rabies vaccination are both recommended if the exposed individual has not previously been vaccinated against rabies. RabIg will provide immediate protection while the patient's immune response to the vaccine develops. People who have been previously vaccinated against rabies (either as pre-exposure prophylaxis or previous post-exposure prophylaxis) require only 2 doses of rabies vaccine (and no RabIg) for post-exposure management.

When RabIg is required, a maximum dose of 20 IU/kg should be given in all age groups. As much as possible of the RabIg should be thoroughly infiltrated into the wound(s) and surrounding area. Using a separate needle, any remaining volume of RabIg should be injected intramuscularly at a site distant from the site of vaccine administration. If the location of the wound cannot be determined – as is the case with some bat bites – administer the entire dose intramuscularly. When administering RabIg and the rabies vaccine at the same time, a separate needle, syringe, and anatomical injection site must be used. If it is not possible to administer RabIg concurrently with rabies vaccine, RabIg should still be administered up to 7 days after the vaccine series is initiated.

Additional details on the use of RabIg can be found in the *Rabies Vaccines chapter* of the *Canadian Immunization Guide*.

Pocket Guide for Immunizers:

Pooled Polyclonal Immunoglobulin Products

Varicella Immunoglobulin (VarIg)

Routine varicella vaccination is the most important method of chickenpox prevention. However, varicella vaccine is a live attenuated vaccine and therefore is contraindicated in pregnancy or in those with some immunocompromising conditions.

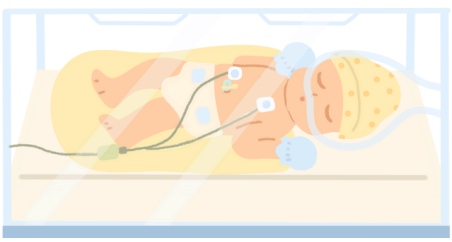
The *Varicella (Chickenpox) Vaccines chapter* of the *Canadian Immunization Guide* provides criteria to determine when an exposure to chickenpox or herpes zoster (shingles) is considered significant, as well as criteria for determining who is considered susceptible to chickenpox. For post-exposure management, those who did not receive 2 doses of varicella-containing vaccine or who do not have laboratory evidence of immunity to varicella are considered susceptible.

The univalent varicella vaccine is the main product used for post-exposure prophylaxis for susceptible individuals with significant exposures to varicella; the measles, mumps, rubella, and varicella (MMRV) vaccine is not generally used for PEP due to lack of data with respect to its use for post-exposure management. If the susceptible, exposed individual is at increased risk of severe varicella and immunization with univalent varicella vaccine is contraindicated, VarIg is recommended instead. People considered at increased risk for severe varicella if they are susceptible – for whom the univalent varicella vaccine is generally not recommended – are as follows:

- anyone who is pregnant;
- immunocompromised individuals, including recipients of hematopoietic stem cell transplantation (they should receive post-exposure prophylaxis regardless of pre-transplant immunization or infection history);
- newborns whose mother or birthing parent had chickenpox from 5 days before to 48 hours after delivery; and
- premature infants (born at less than 28 weeks gestation or weighing less than 1,000 grams at birth) who are in intensive care settings.

When indicated for significant exposures, VarIg should be administered immediately, but no later than 96 hours after first chickenpox or shingles exposure. For prolonged exposures, VarIg can be administered within 96 hours from last exposure. If more than 96 hours but fewer than 10 days have passed since last exposure, VarIg can still be used, but its primary purpose is to attenuate the disease, not to prevent it.

See the *Varicella (Chickenpox) Vaccines chapter* of the *Canadian Immunization Guide* for additional details.



Human immunoglobulin (Ig)

Human immunoglobulin (Ig) can be administered to provide continuous passive immunization or immunomodulation in certain diseases that limit the natural functioning of the immune system. These ongoing therapeutic uses are outside the scope of this pocket guide.

Administration of Ig as post-exposure prophylaxis has been used to reduce the risk of measles and hepatitis A infections.

Two types of Ig preparations that may be used in Canada for measles post-exposure prophylaxis (PEP) are:

- intramuscular immunoglobulin (IMIg) – human immunoglobulin that is administered intramuscularly, and
- intravenous immunoglobulin (IVIg) – human immunoglobulin that is administered intravenously.

IMIg may also be used for pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) for hepatitis A. GamaSTAN® is the only IMIg preparation available in Canada. Please see Table 1 for more information on available IVIg products.

Use of Human Immunoglobulin for Measles

Routine immunization with measles-containing vaccine (measles, mumps, and rubella [MMR] or measles, mumps, rubella, and varicella [MMRV]) is the most important method of preventing measles infection and outbreaks. However, MMR and MMRV are live attenuated vaccines and therefore are generally contraindicated in pregnancy; as well, administration to those who are immunocompromised should involve approval from their attending physician, who will consider their type of immunodeficiency and degree of immunosuppression.

The *Measles Vaccines chapter* of the *Canadian Immunization Guide* provides criteria to determine measles immunity and susceptibility. For healthy, immunocompetent people 6 months of age and older who are susceptible to measles, with the exception of anyone who is pregnant, administration of MMR vaccine is recommended as soon as possible, but within 72 hours after a measles exposure. Human immunoglobulin should be considered for post-exposure measles prophylaxis in select susceptible individuals for whom MMR vaccine is generally not recommended, as follows:

- anyone who is pregnant;
- infants under 6 months of age; and
- immunocompromised individuals (please see Table 3 in the *Updated recommendations on measles post-exposure prophylaxis* document from the National Advisory Committee on Immunization (NACI) for in-depth guidance on who should, and who should not, receive measles PEP based on the type of immunocompromising condition they have or the type of immunosuppressive therapy they are receiving).

As well, human immunoglobulin should be considered for susceptible immunocompetent infants between 6 and 11 months of age who present between 73 hours and 6 days after measles exposure (i.e., too late to receive measles-containing vaccine for PEP).

Use of IMIg

The dose of IMIg is 0.5 ml/kg IM to a maximum of 15 mL. Volumes greater than 2 mL for children or 3 to 5 mL for adults should be divided and injected at 2 or more sites. IMIg is the human immunoglobulin product recommended for infants. For older individuals needing human immunoglobulin, it should be noted that those weighing 30 kg or more should not receive IMIg except in extenuating circumstances, using clinical discretion (e.g., in remote settings where administering or accessing IVIg may not be feasible). Please see Table 3 for more information about IMIg dosing considerations for measles PEP.

Use of IVIg

IVIg at a dose of 400 mg/kg IV should be considered for those for whom human immunoglobulin is indicated who weigh 30 kg or more, or for whom IMIg injection volume is a concern (including children). IVIg requires administration in hospital with appropriate staff supervision over several hours.

As administering IVIg for measles PEP is both time and resource intensive, in cases where it is suspected or possible that the exposed individual has prior immunity to measles, serologic testing should be considered to avoid the unnecessary administration of IVIg. Serologic testing should be used only if test results can be obtained within 24 hours.

See the *Measles Vaccines chapter* of the *Canadian Immunization Guide* for more details, including Table 2.

Use of Human Immunoglobulin for Hepatitis A

Immunization with hepatitis A vaccine is the most important method of both pre-exposure prevention and post-exposure prophylaxis against hepatitis A.

For pre-exposure prevention, IMIg may be used for short-term protection against hepatitis A (such as before travel):

- for those who cannot receive the hepatitis A vaccine (i.e., infants less than 6 months age; those with a history of anaphylaxis to the hepatitis A vaccine or its components); OR
- in addition to the hepatitis A vaccine in those who are immunocompromised.

For post-exposure prophylaxis, IMIg may be considered for susceptible groups:

- in which hepatitis A vaccine is contraindicated (i.e., infants under 6 months of age; those with a history of anaphylaxis to hepatitis A vaccine or its components);
- in conjunction with hepatitis A vaccine in those for whom hepatitis A vaccine could have lower effectiveness and/or hepatitis A infection can have more severe consequences (i.e., susceptible immunocompromised individuals or those with chronic liver disease);
- in conjunction with hepatitis A vaccine for susceptible adults aged 60 years and older who are close or household contacts of an individual with hepatitis A, as this age group is at increased risk of severe disease and may have reduced vaccine response; OR
- when the hepatitis A vaccine is unavailable.

IMIg is optimally given as soon as possible after exposure. Its benefit beyond 14 days from the last exposure is unknown.

See the *Hepatitis A Vaccines chapter* of the *Canadian Immunization Guide* for more details, including guidance on who is considered susceptible to hepatitis A infection.

Dosage, route, and timing of administration of immunoglobulin products

Table 3: Summary of dosage, route and timing of administration of immunoglobulin products

(Source: *Canadian Immunization Guide*, unless otherwise specified)

Product	Group (See sections under Recommendations for use of immunoglobulin products in public health for product indications)	Dosage and administration route	Timing of administration[1]
Hepatitis B immunoglobulin (HBIg)	Infants whose birthing parent is infected with hepatitis B	0.5 mL IM	As soon as possible within 12 hours of birth; can be up to 7 days after birth
	Sexual contacts	0.06 mL/kg IM	Within 48 hours of exposure (and up to 14 days with reduced effectiveness)
	Percutaneous or mucosal exposure	0.06 mL/kg IM	Within 48 hours of exposure (and up to 7 days with reduced effectiveness)
Tetanus immunoglobulin (TIg)	< 7 years of age who require TIg for PEP	4 units/kg deep IM, but may be advisable to give the entire vial contents (250 units IM)	As soon as possible after injury, up to 21 days post injury

Pocket Guide for Immunizers:

Pooled Polyclonal Immunoglobulin Products

Product	Group (See sections under Recommendations for use of immunoglobulin products in public health for product indications)	Dosage and administration route	Timing of administration[1]
Tetanus immunoglobulin (TIg)	7 years of age and over who require TIg for PEP	250 units deep IM	As soon as possible after injury, up to 21 days post injury
Rabies immunoglobulin (RabIg)	Those who require RabIg for PEP	20 IU/kg (maximum dose) with as much as possible injected into the wound site, and the remainder given IM using a new needle at a site separate from vaccine	As soon as possible, once a decision is made to administer PEP
Varicella Zoster immunoglobulin (VarIg)	Those who require VarIg for PEP	125 IU/10 kg IM or IV; maximum dose 625 IU; minimum dose 125 IU Source: *product monograph* and the *Updated NACI recommendations for the use of varicella zoster immune globulin (VarIg) for the prevention of varicella in at-risk patients*	Ideally within 96 hours of first exposure, but can be up to 10 days from last exposure; see the section in this document titled Varicella Immunoglobulin (VarIg) for details

Pocket Guide for Immunizers:

Pooled Polyclonal Immunoglobulin Products

Product	Group (See sections under Recommendations for use of immunoglobulin products in public health for product indications)	Dosage and administration route	Timing of administration[1]
Measles Human immunoglobulin administered IM (IMIg)	Those who require IMIg for measles PEP	0.5 mL/kg IM to a maximum of 15 mL[2]; dose volume should be divided if larger than 2 mL for children, or 3 to 5 mL for adults.[3,4]	As soon as possible within 6 days of exposure
Measles Human immunoglobulin administered IV (IVIg)	Those who require IVIg for measles PEP	400 mg/kg IV; requires administration in a hospital with appropriate supervision over several hours	As soon as possible within 6 days of exposure
Hepatitis A Human immunoglobulin administered for post-exposure prophylaxis (PEP)	Those who require IMIg for hepatitis A PEP	0.1 mL/kg IM	As soon as possible, and within 14 days from last exposure

Product	Group (See sections under Recommendations for use of immunoglobulin products in public health for product indications)	Dosage and administration route	Timing of administration[1]
Hepatitis A Human immunoglobulin administered for pre-exposure prophylaxis (PrEP)	Those who require IMIg for hepatitis A PrEP (mostly those who are travelling)	Dependent on duration of travel • Up to 1 month: 0.1 mL/kg • Up to 2 months: 0.2 mL/kg • 2 months and longer: repeat dose of 0.2 mL/kg every 2 months	Before departure and during travel, if travelling for 2 months or longer

Abbreviations: PEP = post-exposure prophylaxis; PrEP = pre-exposure prophylaxis; IMIg = human immunoglobulin administered intramuscularly; IVIg = human immunoglobulin administered intravenously

[1] A vaccine that is required at the same time as immunoglobulin should be administered at a separate anatomical site, using a separate needle and syringe.

[2] More than 15mL of IMIg can be administered for measles PEP to people weighing 30kg or more in extenuating circumstances, using clinical discretion (e.g., in remote settings where administering or accessing IVIg may not be feasible).

[3] While it is recommended that the dose volume for IMIg measles PEP in children should be divided if larger than 2 mL, up to 3 mL can be administered, with clinical consideration, to reduce the number of injections needed.

[4] NACI guidance on measles PEP cites a higher dose than what is advised in the GamaSTAN® product monograph.

Who should not receive immunoglobulin products?

Human immunoglobulin (Ig), HBIg and VarIg are contraindicated in persons with history of anaphylaxis after previous administration of the product, or in persons with proven immediate/anaphylactic hypersensitivity to any component of the product or its container. However, in cases where Ig, HBIg, or VarIg are indicated in someone with a previous anaphylactic reaction to

any of these immunizing agents or their product components, an allergist or an individual with expertise in the diagnosis of anaphylaxis should be consulted.

If Tig is indicated in someone with a previous anaphylactic reaction, assess the risks and benefits; if the product is used, ensure it is in a controlled, closely monitored setting (such as an emergency room with the appropriate personnel and equipment available to manage anaphylaxis). Given the importance of preventing rabies, there are no contraindications to the use of RabIg if it is indicated, but those with a past anaphylactic reaction to receipt of immunoglobulin should be administered RabIg in a controlled, closely monitored setting, and expert opinion should be sought.

In situations of suspected previous hypersensitivity or non-anaphylactic allergy to product components, 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 in a controlled, closely monitored setting. For more information about administering human Ig preparations to people with isolated IgA deficiency, please visit the Canadian Blood Services website.

Are there concerns regarding the timing of administering vaccines and immunoglobulin products?

Immunoglobulins can interfere with the response with the following live attenuated vaccines: MMR, MMRV, and univalent varicella vaccines. If these vaccines are given 2 weeks or more before the immunoglobulin was received, then interference should not occur. The *Blood Products, Human Immunoglobulin and Timing of Immunization chapter* of the *Canadian Immunization Guide* provides guidelines for how long to wait following administration of various immunoglobulin products to receive the MMR, MMRV, or univalent varicella vaccines.

What are the side effects associated with immunoglobulin products?

Severe adverse reactions to human immunoglobulin (Ig) and disease-specific immunoglobulin products are extremely rare and include allergic reactions (urticaria, angioedema, anaphylaxis) and potential increase in risk of thrombosis within 24 hours of receipt, especially when immunoglobulin is given in large volumes.

Some short-term mild to moderate reactions are more commonly seen and can include:

- local pain, erythema and stiffness of muscles at the injection site
- mild fever or malaise
- flushing, headache, chills, and nausea