

PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

IMOGRAM[®] Rabies Pasteurized

Rabies Immune Globulin, Pasteurized (Human)

Solution for Injection (150 IU/mL)

2.0 mL vials and 10.0 mL vials

Passive Immunizing Agent for the Prevention of Rabies

ATC: Code J06BB05

Manufactured by:
Sanofi Pasteur SA
Lyon, France

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IMOGRAM[®] Rabies Pasteurized

Rabies Immune Globulin, Pasteurized (Human)

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration

Intramuscular

Dosage Form/Strength

Solution for injection.

Each 1.0 mL is formulated to contain:

Active Ingredient

Human proteins (100-160 mg) containing IgG-class human rabies immune globulins with a minimum titre of 150 IU/mL.

Clinically Relevant Non-medicinal Ingredients

Glycine

IMOGRAM[®] Rabies Pasteurized is supplied in 2 mL vials (300 IU) and 10 mL vials (1,500 IU).

For a complete listing see [DOSAGE FORMS, COMPOSITION AND PACKAGING](#).

DESCRIPTION

IMOGRAM[®] Rabies Pasteurized [Rabies Immune Globulin (RIG), Pasteurized (Human)] is a sterile solution of antirabies immune globulins (10-16% protein) for intramuscular administration.

INDICATIONS AND CLINICAL USE

IMOGRAM[®] Rabies Pasteurized is indicated for post-exposure prophylaxis in persons suspected of exposure to rabies, who have not previously received a complete immunization regimen with a cell culture produced rabies vaccine.

Persons previously vaccinated with other types of rabies vaccines in whom adequate antibody levels have not been demonstrated should receive full post-exposure prophylaxis with RIG and a cell culture-produced rabies vaccine.

IMOGRAM[®] Rabies Pasteurized should be administered promptly after exposure, in conjunction with rabies vaccine. If IMOGRAM[®] Rabies Pasteurized is not administered as recommended at the

initiation of the post-exposure rabies vaccine series, it can be administered up to seven days following the first dose of the rabies vaccine. Since rabies vaccine-induced antibody begins to appear within one week, there is no value in administering rabies immune globulin more than seven days after rabies vaccination has begun. (1) (2) (3)

Recommendations for passive and/or active immunization after exposure to an animal suspected of having rabies have been outlined by the National Advisory Committee on Immunization (NACI), the Advisory Committee on Immunization Practices (ACIP), and the World Health Organization (WHO). (1) (2) (3) (4) (5) (6)

Post-Exposure Prophylaxis

A decision on the management of a person who has been exposed to the risk of rabies infection must be made rapidly and judiciously, since delay in starting post-exposure prophylaxis reduces its effectiveness, and the disease once established is almost always fatal. (1)

Rabies prophylaxis must be considered in every incident where potential exposure to rabies virus has occurred. The following factors should be reviewed when considering the need for post-exposure management. (1)

A. Species of animal

The animals in Canada most often proven rabid are wild and domestic mammals (skunks, foxes, raccoons, bats, cattle and stray dogs and cats). As the distribution of animal rabies and the species involved vary considerably across Canada, it is important to consult local public health officials. Human exposures to livestock are usually confined to salivary contamination, with the exception of horses and swine in which biting incidents have been reported. Risk of infection following exposure to rabid cattle is low. Squirrels, hamsters, guinea-pigs, gerbils, chipmunks, rats, mice, other rodents, and rabbits and hares are rarely found to be infected with rabies and are not known to cause human rabies in Canada and the United States. Post-exposure prophylaxis should be considered if the behaviour of these animals was highly unusual. (1)

B. Type of exposure

Rabies is transmitted when the virus in the saliva is introduced into a bite wound, open cuts in skin, or onto mucous membranes such as the mouth or eyes. Bites from an infected animal are the main route of exposure. Transmission has also been reported through transplantation of organs from undiagnosed infected persons. (1)

There are three broad categories of exposures – bite exposure, non-bite exposure and bat exposure, as described below:

- 1) **Bite exposure:** Any penetration of skin by teeth. Bites inflicted by most animals are readily apparent, with the exception of bats (see ‘Bat exposure’).
- 2) **Non-bite exposure:** Contamination of scratches, abrasions or cuts of skin or mucous membranes by saliva or other potentially infectious material, such as the brain tissue of a rabid animal. Petting a rabid animal, handling blood, urine or feces of a rabid animal, and being sprayed by a skunk are not considered as exposure and hence do not warrant post-exposure prophylaxis.

Post-exposure prophylaxis is recommended in rare instances, such as inhalation of aerosolized virus by spelunkers exploring caves inhabited by infected bats or by laboratory technicians homogenizing tissues infected with rabies virus. However, the efficacy of prophylaxis after such exposures is not proven. Stringent guidelines concerning the suitability of tissue donors have eliminated the probability that rabies virus will be transmitted iatrogenically.

Exposures incurred while caring for humans with rabies could in theory occur. There are no documented cases of this type of transmission, but post-exposure prophylaxis should be considered upon exposure to saliva or neural tissue from a person with rabies. (1)

- 3) Bat exposure: Post-exposure prophylaxis is only recommended in cases of a direct contact with a bat where a bite, scratch, or saliva exposure into a wound or mucous membrane cannot be ruled out. Since it is very difficult to ascertain whether a bat bite has taken place, post-exposure prophylaxis is generally recommended. (5)**

C. Circumstances of exposure

Each incident requires full investigation including an assessment of the risk of rabies in the animal species involved and the behaviour of the particular animal. An **unprovoked** attack is more likely to indicate that the animal is rabid. Nevertheless, rabid animals may become uncharacteristically quiet. Bites inflicted on a person attempting to feed or handle an apparently healthy animal should generally be regarded as **provoked**. (1)

D. Vaccination status and behaviour of the animal

Domestic pets (dogs, cats, ferrets) with up-to-date rabies vaccination are unlikely to become rabid. Persons with bite exposures should consult a veterinarian to determine the vaccination status of the animal. A history of abnormal or aggressive behaviour in a domestic animal, a potential for exposure to animals that could transmit rabies, and a previous encounter with a wild animal should be considered when determining the likelihood that a domestic animal exposure carries a risk of rabies transmission. (1)

E. Age of exposed person

Exposure history reports obtained from children can be difficult to interpret and is potentially unreliable; this must be taken into consideration for appropriate post-exposure management. (1)

F. Location and severity of the bite

Once the rabies virus is inoculated into a wound, it is taken up at a nerve synapse and travels to the brain causing fatal encephalitis. Post-exposure prophylaxis is ineffective after the rabies virus has invaded the nervous system. Bites at a location where there is a higher density of nerve endings (hands and face) have increased risk of developing rabies encephalitis and are considered high-risk exposures. More severe bites are more likely to indicate that the animal is rabid, and increase the risk of rabies transmission due to greater exposure to saliva. (1)

Management of Persons Post-Exposure

The following recommendations are intended as a guide for the management of persons following possible exposure to rabies and may need to be modified in accordance with the specific circumstances of the exposure to rabies. (1)

- A. **Local treatment of wounds: Immediate and thorough cleaning and flushing of the wound with soap and water is imperative and is probably the most effective procedure in the prevention of rabies.** Suturing the wound should be avoided if possible. Tetanus prophylaxis and antibacterial drugs should be given as required. (1)
- B. **Immunizing agents:** There are two types of immunizing products:
- 1) **Rabies Vaccines** which contain inactivated virus and induce an active immune response within 7 to 10 days post-vaccination that persists for at least one year after completion of a course of recommended vaccination schedule;
 - 2) **Rabies Immune Globulin (RIG)** which provides rapid protection for a short period of time (half-life about 21 days).

Rabies vaccine and RIG should be used concurrently for optimum post-exposure prophylaxis against rabies, except in persons previously vaccinated with a cell culture produced-rabies vaccine. (1)

Post-Exposure Prophylaxis Guide

Table 1 summarizes post-exposure prophylaxis for persons potentially exposed to rabies. (1)

Table 1: Post-exposure prophylaxis for persons potentially exposed to rabies by animal type

Animal species	Condition of animal at time of exposure	Management of exposed person	
		Not previously immunized against rabies	Previously immunized against rabies
Dog, cat or ferret	Healthy and available for a 10-day observation period	<ol style="list-style-type: none"> 1. Local treatment of wound. 2. At first indication of rabies in animal, give RIG and start rabies vaccine (produced in cell culture). 3. At first indication of rabies in animal, arrange for testing of animal for rabies. 	<ol style="list-style-type: none"> 1. Local treatment of wound. 2. At first indication of rabies in animal, start rabies vaccine (produced in cell culture). 3. At first indication of rabies in animal, arrange for testing of animal for rabies.
	Unknown or escaped	<ol style="list-style-type: none"> 1. Local treatment of wound. 2. Consult public health officials for risk assessment. 	
	Rabid or suspected to be rabid*	<ol style="list-style-type: none"> 1. Local treatment of wound. 2. Give RIG and start rabies vaccine (produced in cell culture). 3. Arrange for testing of animal for rabies. 	<ol style="list-style-type: none"> 1. Local treatment of wound. 2. Start rabies vaccine (produced in cell culture). 3. Arrange for testing of animal for rabies.
Skunk, bat, fox, coyote, raccoon and other wildlife	Regard as rabid unless geographic area is known to be rabies-free*	<ol style="list-style-type: none"> 1. Local treatment of wound. 2. Give RIG and start rabies vaccine (produced in cell culture) immediately. 3. Arrange for testing of animal for rabies. 	<ol style="list-style-type: none"> 1. Local treatment of wound. 2. Start rabies vaccine (produced in cell culture) immediately. 3. Arrange for testing of animal for rabies.
Livestock, rodents, hares or rabbits	Consider individually. Consult public health officials. Bites from small rodents (squirrels, chipmunks, rats, mice, hamsters, gerbils, guinea pigs) and rabbits and hares only warrant post-exposure prophylaxis if the behaviour of the animal was highly unusual. Bites from larger rodents (ground hogs/woodchucks, beavers) require risk assessment.		

RIG: Rabies Immune Globulin

*If possible, the animal should be humanely euthanized and the brain tested for rabies as soon as possible. Holding for observation is not recommended. Discontinue rabies vaccine series if rabies testing of the involved animal is negative.

CONTRAINDICATIONS

IMOGRAM[®] Rabies Pasteurized should not be administered as repeat doses once rabies vaccination has been initiated. Repeating the dose may interfere with maximum active immunity expected to develop from the rabies vaccine. (1)

There is no contraindication to the use of IMOGRAM[®] Rabies Pasteurized if indicated following exposure to a proven rabid animal. (1)

WARNINGS AND PRECAUTIONS

General

Before administration of IMOGRAM[®] Rabies Pasteurized, healthcare professionals should inform the recipient or their parent or guardian of the benefits and risks of immunization, inquire about the recent health status of the recipient, review the recipient's history concerning possible hypersensitivity to the product or similar products, previous immunization history, the presence of any contraindication to immunization and comply with any local requirements regarding information to be provided to the recipient, parent or guardian before immunization. (1)

IMOGRAM[®] Rabies Pasteurized is made from human plasma. The risk that this product may transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and/or removing certain viruses. An alcohol fractionation procedure, which is used to purify the immune globulin component, removes and/or inactivates both enveloped and non-enveloped viruses. An added heat treatment process (60°C, for 10-11 hours) further inactivates both enveloped and non-enveloped viruses. Despite these measures, it is still theoretically possible that known or unknown infectious agents may be present.

Administration-Route Related

Infiltration of wounds in some anatomical sites (finger tips) must be carried out with care in order to avoid increased pressure in the tissue compartment (compartment syndrome).

IMOGRAM[®] Rabies Pasteurized should be administered intramuscularly.

Do not administer IMOGRAM[®] Rabies Pasteurized by intravascular injection; ensure that the needle does not penetrate a blood vessel. See DOSAGE and ADMINISTRATION.

Under no circumstances should RIG be administered in the same syringe or at the same site as the rabies vaccine. (1)

Hematologic

IMOGRAM[®] Rabies Pasteurized has not been evaluated in persons with thrombocytopenia or bleeding disorders. As with any other product administered intramuscularly, the product risk versus benefit for persons at risk of hemorrhage following intramuscular injection must be evaluated. NACI has published recommendations for the immunization of people with hemophilia and other bleeding disorders. (1)

Immune

Hypersensitive individuals should be immunized only under strict medical supervision. (1)

Although systemic reactions to immunoglobulin preparations are rare, the possibility of allergic reactions in individuals sensitive to components of the product should be evaluated. **Epinephrine hydrochloride solution (1:1000) and other appropriate agents should be available for immediate use in case an anaphylactic or acute hypersensitivity reaction occurs.** Healthcare professionals should be familiar with the current recommendations for the initial management of anaphylaxis in non-hospital settings, including the proper use of anaphylaxis management kits. For instructions on recognition and treatment of anaphylactic reactions, see the current edition of the Canadian Immunization Guide or visit the Health Canada website. (1)

IMOGAM[®] Rabies Pasteurized should be given with caution to patients with a history of prior systemic allergic reactions following the administration of human immune globulin preparations.

Persons with specific IgA deficiency have increased potential for developing antibodies to IgA and could have anaphylactic reactions to subsequent administration of blood products containing IgA. (7) (8)

Special Populations

Pregnant women

Pregnancy is not a contraindication to rabies post-exposure prophylaxis.

The safety of IMOGAM during pregnancy has not been established by controlled clinical trials. Animal reproduction studies have not been conducted with IMOGAM[®] Rabies Pasteurized. It is also not known whether IMOGAM[®] Rabies Pasteurized can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. As rabies is fatal, IMOGAM[®] Rabies Pasteurized should be given to a pregnant woman if clearly needed. (1) (2)

Based on limited data, there have been no fetal abnormalities associated with rabies immunization. Clinical experience with other immune globulin preparations suggests that there are no known adverse effects on the fetus from immune globulin, but there are no reported studies indicating whether or not such adverse effects occur.

Nursing women

Immune globulins have been reported to be excreted in maternal milk. Lactation is not a contraindication to rabies post-exposure prophylaxis. As rabies is fatal, IMOGAM[®] Rabies Pasteurized should be given to a nursing woman if clearly needed. (1) (2)

ADVERSE REACTIONS

In a double-blind controlled clinical trial, 64 volunteers were randomized into the following four treatment groups: IMOGAM[®] Rabies Pasteurized + IMOVAX[®] Rabies; IMOGAM[®] RABIES (non-heat treated) + IMOVAX[®] Rabies; IMOGAM[®] Rabies Pasteurized + placebo; IMOGAM[®] RABIES (non-heat treated) + placebo. Two subjects reported severe headaches, one in the IMOGAM[®] Rabies Pasteurized + placebo group and one in the IMOGAM[®] Rabies (non-heat treated) + IMOVAX[®] Rabies group. One third of the volunteers reported moderate systemic

reactions (headache and malaise). These were equally distributed among the 4 treatment groups with no significant differences between the groups. (9) (10)

The adverse events listed below have been compiled from a clinical trial and post-market experience with IMOGAM[®] Rabies Pasteurized. (11)

Cardiac disorders

Hypotension
Tachycardia

Gastrointestinal disorders

Nausea
Vomiting

General disorders and administration site conditions

Local reaction
Fever, chills

Immune system disorders

Allergic type reaction
Anaphylactic shock

Skin and subcutaneous system disorders

General pruritus
Rash

Physicians, nurses, and pharmacists should report any adverse occurrences temporally associated with the administration of the product in accordance with local requirements and to the Global Pharmacovigilance Department, Sanofi Pasteur Limited, 1755 Steeles Avenue West, Toronto, ON, M2R 3T4, Canada. 1-888-621-1146 (phone) or 416-667-2435 (fax).

DRUG INTERACTIONS

Concomitant Vaccine Administration

Live virus vaccines, such as measles vaccine, should not be given for four months following IMOGAM[®] Rabies Pasteurized administration because antibodies in the immune globulin preparation may interfere with the immune response to the vaccine. If administration of IMOGAM[®] Rabies Pasteurized becomes necessary within two weeks after receiving a live attenuated viral vaccine, vaccination may have to be repeated.

DOSAGE AND ADMINISTRATION

Recommended Dose and Dosage Adjustment

IMOGAM[®] Rabies Pasteurized should be used in conjunction with a rabies cell-culture produced vaccine. The recommended dose of IMOGAM[®] Rabies Pasteurized is 20 IU/kg (0.133 mL/kg) of body weight at the time of administration of the first dose of rabies vaccine. (1) (12) (13) (See [INDICATIONS AND CLINICAL USE](#))

The dose of 20 IU/kg of body weight is the same for children and adults. The dose of IMOOGAM[®] Rabies Pasteurized, especially following multiple wounds, may be diluted 2- to 3-fold in a solution of 0.9% sodium chloride in order to provide the full amount of human rabies immunoglobulin required for appropriate infiltration of wounds and surrounding area. (14) (15)

Administration

Inspect for extraneous particulate matter and/or discolouration before use. (See [DOSAGE FORMS, COMPOSITION AND PACKAGING](#)). If these conditions exist, the product should not be administered.

Do not remove either the stopper or the metal seal holding it in place. Cleanse the vial stopper with a suitable germicide. Aseptic technique must be used. Use a separate sterile needle and syringe, or a sterile disposable unit, for each individual recipient to prevent disease transmission. Needles should not be recapped and should be disposed of according to biohazard waste guidelines.

Before injection, the skin over the site to be injected should be cleansed with a suitable germicide.

IMOOGAM[®] Rabies Pasteurized should be administered intramuscularly.

Do not administer IMOOGAM[®] Rabies Pasteurized by intravascular injection; ensure that the needle does not penetrate a blood vessel.

If anatomically feasible, the full dose of RIG should be thoroughly infiltrated in the area around and into the wounds. Any remaining volume should be injected intramuscularly at a site distant from rabies vaccine administration. (1)

IMOOGAM[®] Rabies Pasteurized should never be administered in the same syringe or into the same anatomical site as the rabies vaccine. Because IMOOGAM[®] Rabies Pasteurized may partially suppress active immunity to the rabies vaccine, no more than the recommended dose should be given. (1)

Do not inject intravenously.

Give the patient a permanent immunization record. In addition, it is essential that the healthcare professional records the immunization history in the permanent medical record of each patient. This permanent office record should contain the name of the product, date given, dose, manufacturer and lot number.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Pharmacodynamics

Mechanism of Action

IMOOGAM[®] Rabies Pasteurized provides passive protection by neutralizing the rabies virus when given to individuals exposed to rabies virus. (16)

Duration of Effect

Rabies Immune Globulin (Human) of adequate potency has been used in conjunction with rabies vaccine of duck embryo origin. When a rabies immune globulin dose of 20 IU/kg was given simultaneously with the first dose of rabies vaccine, levels of passive anti-rabies antibody were detected 24 hours after injection in all individuals. There was minimal or no interference with the immune response to the initial and subsequent doses of rabies vaccine, including booster doses. (12) (17)

STORAGE AND STABILITY

IMOOGAM[®] Rabies Pasteurized should be stored at refrigerator temperature (2° C to 8° C). **Do not freeze.** Products that have been exposed to freezing should not be used. IMOOGAM[®] Rabies Pasteurized contains no preservatives, and unused portions must be discarded immediately.

Do not use after expiration date.

SPECIAL HANDLING INSTRUCTIONS

Do not heat by placing in warm water or incubator.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage Forms

IMOOGAM Rabies Pasteurized is supplied as a clear or slightly opalescent, colourless or pale-yellow or light-brown liquid ready for intramuscular injection. During storage it may show formation of slight turbidity or a small amount of visible particulate matter.

Composition

The product is standardized against a Standard Rabies Immune Globulin of known potency in International Units (IU) for rabies antibody. Each vial is formulated to contain at least 150 IU per millilitre (IU/mL).

Each mL contains:

Active ingredient

Human proteins containing (IgG-class) human rabies immune globulins with a minimum titre of 150 IU^{*}/mL 100-160 mg

Other ingredients

Glycine 22.5 mg
Sodium chloride 1 mg
Water for injection up to 1 mL

** Titre determined by the Rapid Fluorescent Focus Inhibition Test (RFFIT) technique.*

IMOGRAM[®] Rabies Pasteurized is preservative-free.

Packaging

IMOGRAM[®] Rabies Pasteurized is supplied in vials with a minimum potency of 150 IU/mL. The vials are made of Type I glass. The container closure system does not contain latex (natural rubber).

IMOGRAM[®] Rabies Pasteurized is available in a package of:

2 mL Vial - 300 IU (150 IU/mL) - which is sufficient for a child weighing 15 kg

10 mL Vial - 1,500 IU (150 IU/mL) - which is sufficient for an adult weighing 75 kg

Vaccine Information Service: 1-888-621-1146 or 416-667-2779. Business Hours: 7:30 a.m. to 7:30 p.m. Eastern Time, Monday to Friday.

Full product monograph available on request or visit us at www.sanofipasteur.ca

Product information as of November 2015.

Manufactured by:
Sanofi Pasteur SA
Lyon, France

Distributed by:
Sanofi Pasteur Limited
Toronto, Ontario, Canada

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PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

IMOGRAM[®] Rabies Pasteurized [Rabies Immune Globulin, Pasteurized (Human)] is a sterile solution of human proteins (10-16 % protein) containing anti-rabies immune globulins (IgG class) with a minimum titre of 150 IU/mL, for intramuscular injection.

Product Characteristics

IMOGRAM[®] Rabies Pasteurized is a clear or slightly opalescent, colourless or pale-yellow or light-brown liquid. During storage it may show formation of slight turbidity or a small amount of visible particulate matter.

IMOGRAM[®] Rabies Pasteurized is prepared by cold alcohol fractionation from pooled venous plasma of individuals immunized with rabies vaccine prepared in human diploid cells (Human Diploid Cell Vaccine, HDCV). The product is stabilized with 0.3 M glycine. The globulin solution has a pH of 6.8 ± 0.4 adjusted with sodium hydroxide or hydrochloric acid. No preservatives are added.

Viral Inactivation

A heat-treatment process step (58° to 60° C, for 10-11 hours) to inactivate viruses has been added to further reduce risk of blood-borne viral transmission. The inactivation and removal of model and laboratory strains of enveloped and non-enveloped viruses during the manufacturing and heat treatment processes for IMOGRAM[®] Rabies Pasteurized has been validated by spiking experiments. Human immunodeficiency virus, type 1 (HIV-1) and type 2 (HIV-2) were selected as relevant viruses for plasma derived products. Bovine viral diarrhea virus and Sindbis virus were chosen to model hepatitis C virus. Porcine pseudorabies virus was selected to model hepatitis B virus and herpes virus. Avian reovirus was used to model non-enveloped RNA viruses and for its relative resistance to inactivation by chemical and physical methods. Finally, porcine parvovirus was selected to model human parvovirus B19 and its notable resistance to inactivation by heat treatment.

Removal and/or inactivation of the studied enveloped and non-enveloped model viruses was demonstrated at the precipitation III stage of manufacturing. In addition, inactivation was demonstrated to occur during the heat treatment process for the studied enveloped and non-enveloped viruses.

CLINICAL TRIALS

Studies with IMOGRAM[®] Rabies Pasteurized administered with the first of five doses of Inactivated Human Rabies Vaccine Mérieux confirmed that passive immunization with 20 IU/kg

of Rabies Immune Globulin (Human) provides maximum circulating antibody with minimum interference with the active immunization.

A recent study indicates that the neutralizing antibody levels following administration of IMOOGAM[®] Rabies Pasteurized, with and without rabies vaccine (HDCV), are not significantly different from that observed following IMOOGAM[®] RABIES (non-heat treated) administered in the same manner. (18)

A controlled double-blind trial was conducted in 64 healthy volunteers randomized into 4 parallel groups consisting of 16 subjects each, to compare the safety and antibody levels achieved following IMOOGAM[®] Rabies Pasteurized and IMOOGAM[®] RABIES (non-heat treated). Each immune globulin was administered either with the rabies vaccine (IMOVAX[®] Rabies) or with a placebo using the standard 5-dose post-exposure prophylactic schedule on days 0, 3, 7, 14, and 28. (9) (10)

The immune globulin dosage corresponded to the post-exposure recommended dose of 20 IU/kg and was administered in three equally divided intramuscular injections of under 5 mL in the gluteus. Serum rabies antibody levels were assessed before treatment and on days 3, 7, 14, 28, 35, and 42 using the Rabies Fluorescent Focus Inhibition Test (RFFIT). (9) (10)

Serum antibody levels were similar in the IMOOGAM[®] Rabies Pasteurized and IMOOGAM[®] RABIES (non-heat treated) groups. By day three, 60% of each group had detectable antibody titers of ≥ 0.05 IU/mL. By day 14, the geometric mean titers (with 95% confidence interval) were 19 IU/mL (11-38) in the IMOOGAM[®] Rabies Pasteurized + vaccine group and 31 IU/mL (20-48) in the IMOOGAM[®] RABIES (non-heat treated) + vaccine group. These differences were not statistically different. (9) (10)

Both IMOOGAM[®] Rabies Pasteurized and IMOOGAM[®] RABIES were safe, and no serious adverse events or allergic reactions were reported. (9) (10)

ADDITIONAL RELEVANT INFORMATION

Rabies virus is classified in the *Rhabdoviridae* family. (4)

Infection with rabies virus characteristically produces an acute illness with rapidly progressive central nervous system manifestations, including anxiety, dysphagia, and convulsions, and almost invariably progresses to death. Some patients may present with paralysis. (4)

Rabies virus is usually transmitted by the bite of a rabid animal, but it can occasionally penetrate abraded skin contaminated with the saliva of infected animals. Progress of the virus after exposure is believed to follow a neural pathway, and the time between exposure and clinical rabies is a function of the proximity of the bite (or abrasion) to the central nervous system and the dose of virus injected. The incubation period is usually 3 to 8 weeks but can be longer. After severe bites to the face, neck or arms, it may be as short as 10 days. After initiation of the rabies vaccination series (cell culture-produced vaccine), it takes approximately one week for the development of anti-rabies antibodies. Therefore, the value of immediate passive immunization with rabies antibodies in the form of RIG cannot be overemphasized. (1)

Regional differences exist in the prevalence of animal rabies and the specific species infected in each region. Between 2006 and 2010, a total of 1005 cases of confirmed animal rabies were

reported in Canada. The species most commonly identified as having rabies by region are as follows: foxes in the Northwest Territories/Nunavut; skunks in Manitoba and Saskatchewan; bats in British Columbia, Alberta, Quebec and Ontario. (1) Although domestic dogs and cats account for less than 10% of reported animal rabies, bites of these species account for the vast majority of suspected rabies exposures in humans and thus the majority of courses of anti-rabies post-exposure treatment. (1)

Airborne transmission has been reported in the laboratory and in bat-infected caves. Transmission has also occurred by transplantation of corneas from patients dying of undiagnosed rabies. Person-to-person transmission by bite has not been documented, although the virus has been isolated from the saliva of patients. (1)

The incubation period in humans ranges from several days to years, with the usual incubation period being 3 to 8 weeks. (1)

Between 1924 and 2009, 24 persons have died of rabies in Canada. Even though disease may not develop in everyone bitten by a rabid animal, a decision on the management of a person who may have been exposed to rabies virus must be made rapidly and judiciously since delay in starting post-exposure prophylaxis reduces its effectiveness. Since it is not possible to distinguish between those in whom rabies will or will not develop if untreated and since the infection is almost always fatal, it is essential that all persons exposed to proved or suspected rabid animals be given post-exposure prophylaxis. (1)

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Vaccine Information Service: 1-888-621-1146 or 416-667-2779. Business Hours: 7:30 a.m. to 7:30 p.m. Eastern Time, Monday to Friday.

Full product monograph available on request or visit us at www.sanofipasteur.ca

Product information as of November 2015.

Manufactured by:
Sanofi Pasteur SA
Lyon, France

Distributed by:
Sanofi Pasteur Limited
Toronto, Ontario, Canada

R5-1115 Canada

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

IMOOGAM[®] Rabies Pasteurized

Rabies Immune Globulin, Pasteurized (Human)

Read this carefully before you start taking IMOOGAM[®] Rabies Pasteurized. This leaflet is a summary and will not tell you everything about this product. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about taking IMOOGAM[®] Rabies Pasteurized.

What is IMOOGAM[®] Rabies Pasteurized used for?

IMOOGAM[®] Rabies Pasteurized contains antibodies to the rabies virus and is used to prevent rabies in persons soon after they have been exposed to the rabies virus. Rabies is a deadly illness that affects the central nervous system. It is caused by the rabies virus which spreads to humans through close contact with the saliva of an infected animal, most often from bites, scratches, or from licks on broken skin or mucous membranes, such as the eyes, nose or mouth.

How does IMOOGAM[®] Rabies Pasteurized work?

IMOOGAM[®] Rabies Pasteurized contains antibodies that neutralize the rabies virus. It provides rapid protection but lasts for only a few weeks. IMOOGAM[®] Rabies Pasteurized is injected in one dose directly into the wound as soon as possible after exposure. A person who is exposed to and has never been vaccinated against rabies should receive IMOOGAM[®] Rabies Pasteurized and rabies vaccinations. IMOOGAM[®] Rabies Pasteurized provides immediate passive protection until the exposed person mounts an immune response to the rabies vaccine.

What are the ingredients in IMOOGAM[®] Rabies Pasteurized?

Medicinal ingredients: human proteins containing anti-rabies antibodies.

Nonmedicinal ingredients: glycine, sodium chloride, water for injection.

IMOOGAM[®] Rabies Pasteurized comes in the following dosage forms:

IMOOGAM[®] Rabies Pasteurized is solution for injection (150 IU/mL), supplied in 2.0 mL and 10.0 mL vials.

Do not use IMOOGAM[®] Rabies Pasteurized if:

- You have previously received IMOOGAM[®] Rabies Pasteurized along with a rabies vaccine.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take IMOOGAM[®] Rabies Pasteurized. Talk about any health conditions or problems you may have, including if you:

- Have an **allergy or hypersensitivity** to any component of the product or the container.
- Are **pregnant or nursing**. It is important that you understand the risks and benefits of using this product. IMOOGAM[®] Rabies Pasteurized should be given to a pregnant or nursing woman only if it is clearly needed. Tell the person giving you the injection if you are pregnant or breast-feeding.
- Have a **bleeding disorder** or take **blood-thinning medications**. Tell the person giving you the injection about your condition. The injection must be done carefully to prevent excessive bleeding.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with IMOOGAM[®] Rabies Pasteurized:

- Live virus vaccines, such as measles vaccine, should not be given for four months following IMOOGAM[®] Rabies Pasteurized.
- IMOOGAM[®] Rabies Pasteurized should not be mixed with the rabies vaccine, other vaccines, or any other medicinal products in the same syringe.

How to take IMOOGAM[®] Rabies Pasteurized:

Usual dose:

A dose of 20 IU/kg of body weight is recommended for children and adults.

IMOOGAM[®] Rabies Pasteurized should be injected into the muscle surrounding the wound.

Overdose:

If you think you have taken too much IMOOGAM[®] Rabies Pasteurized, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

Not applicable.

What are possible side effects from using IMOOGAM[®] Rabies Pasteurized?

These are not all the possible side effects you may feel when taking IMOOGAM[®] Rabies Pasteurized. If you experience any side effects not listed here, contact your healthcare professional. Please also see WARNINGS AND PRECAUTIONS.

An immune globulin product, like any other medicine, may cause serious side effects, such as allergic reactions. The risk of IMOOGAM[®] Rabies Pasteurized causing serious harm is extremely small.

Some people who receive IMOOGAM[®] Rabies Pasteurized may experience the following mild side effects:

- pain or tenderness at the injection site (with redness or swelling).
- fever, headache, or nausea.
- a general feeling of weakness and discomfort.

These side effects usually go away within a few days.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

REPORTING SIDE EFFECTS

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at MedEffect;
- By calling 1-866-234-2345 (toll-free);
- By completing a Patient Side Effect Reporting Form and sending it by:
 - Fax to 1-866-678-6789 (toll-free), or
 - Mail to: Canada Vigilance Program
Health Canada,
Postal Locator 0701E
Ottawa, ON K1A 0K9

Postage paid labels and the Patient Side Effect Reporting Form are available at MedEffect

(<http://hc-sc.ga.ca/dhp-mps/medeff/index-eng.php>).

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store IMOOGAM[®] Rabies Pasteurized in a refrigerator at 2° to 8°C (35° to 46°F). **Do not freeze.** Discard if it has been exposed to freezing.

Protect from light.

Do not use after the expiration date.

Keep out of reach and sight of children.

If you want more information about IMOOGAM[®] Rabies Pasteurized:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the [Health Canada website](http://hc-sc.gc.ca/index-eng.php) (<http://hc-sc.gc.ca/index-eng.php>); the Sanofi Pasteur Limited website (<http://www.sanofipasteur.ca>), or by calling the Sanofi Pasteur Limited Vaccine Information Service at 1-888-621-1146 (no charge) or at 416-667-2779 (Toronto area).

Business hours are 7:30 a.m. to 7:30 p.m.
EST Monday to Friday.

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