Proposed Professional Information

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

Rabigam® IM, 300 IU (150 IU/ml), solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Human rabies immunoglobulin.

Each 2 ml ampoule contains 300 IU (150 IU/ml) of rabies virus antibodies.

Rabigam IM contains immunoglobulin derived from pooled human plasma, sourced from healthy donors, with a high titre of antibodies to the rabies virus.

Each unit of plasma has been individually tested and found non-reactive for hepatitis B surface antigen (HBsAg), antibodies to the hepatitis C virus (HCV) and antibodies to the human immunodeficiency viruses, HIV-1 and HIV-2, using approved methods.

Rabigam IM is prepared by cold ethanol fractionation, to further reduce the risk of viral transmission. In addition, only plasma pools tested and found non-reactive for anti-HIV-1 & -2, HBsAg and anti-HCV by serological testing; and for HIV, HCV, hepatitis B virus (HBV) and hepatitis A virus (HAV) by Nucleic Acid Amplification Techniques (NAT), are used in the manufacture of **Rabigam IM**.

This preparation does not contain any antimicrobial preservatives.

Rabigam IM is sugar free.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection.

The solution is a colourless, pale yellow to light brown liquid exhibiting a slight opalescence. During storage, it may show formation of slight turbidity or a small amount of particulate matter.

Rabigam IM has a pH of between 5,0 - 7,2.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Rabigam IM is indicated as post-exposure prophylaxis of rabies infection for all persons known or suspected to have been exposed to the rabies virus, especially cases of major exposure, in accordance with the WHO recommendations.

Risk Category	Type of Exposure	Action to be taken
I	Touching/feeding animal, licking of skin	None, if case history is reliable. If history is not reliable, treat as for category II.
II	Nibbling of uncovered skin, superficial scratch without bleeding	Apply wound treatment. Administer vaccine. Do not administer anti-rabies immunoglobulin. Stop vaccination if animal is rabies negative on laboratory test, or remains healthy after 10 days observation.
III	Bites/scratches which penetrate the skin and draw blood, licking of mucous membranes or broken skin	Apply wound treatment. Administer vaccine. Administer anti-rabies immunoglobulin. Stop vaccination if animal is rabies negative on laboratory test, or remains healthy after 10 days observation.

WHO Expert Consultation on Rabies, First Report. WHO Technical Report Series 931 2005; WHO, Geneva.

For rabies prevention in category III exposures, combined treatment with immunoglobulin (passive immunisation) and vaccine (active immunisation) is absolutely essential. The only exception is for individuals previously immunised with rabies vaccine and whose antibody titre has been recently confirmed as adequate, who should be treated with the vaccine only.

Rabigam IM must be administered for category III exposures, irrespective of the interval between exposure and initiation of treatment, up to the seventh day after the first dose of vaccine was given.

4.2 Posology and method of administration

Posology

The standard recommended dose is 20 IU per kilogram body mass administered at the same time, but at a different anatomical site, as the vaccine. This dose is applicable to both children and adults. The recommended dose should not be exceeded.

Method of administration

Intramuscular route.

Rabigam IM and the vaccine should be administered at two different sites of the body, using different syringes, to avoid interference with the active antibody response.

Rabigam IM injections should preferably be administered in the bitten site. It should be carefully infiltrated in the depth of, and around the wound if anatomically possible. Any remainder should be injected intramuscularly at a site distant from that used for the rabies vaccine.

The usual recommended site for adults is the deltoid; for infants, the lateral aspect of the thigh is preferable.

If a large volume (>2 ml for children or > 5 ml for adults) is required, it is recommended that this be administered in divided doses at different sites.

If suturing is necessary, ensure that the wound has been adequately infiltrated with **Rabigam IM** locally before suturing.

Note:

- Laboratory diagnosis should not delay initiation of treatment, but failure to detect rabies virus in the offending animal may warrant the halting of treatment.
- Rabies immunoglobulin must be administered as soon as possible (that is, on the day that treatment is started) after suspected exposure to rabies, in conjunction with rabies vaccine.
- If initiation of treatment is delayed for any reason, rabies immunoglobulin should still be given, regardless of the interval between exposure and treatment, up to the seventh day after the first dose of vaccine was given.

For instructions on handling and disposal of this injection, see section 6.6.

4.3 Contraindications

Because of the life-threatening risk due to rabies, there are no contra-indications to the administration of rabies immunoglobulin. **Rabigam IM** is not indicated for patients with proven immunity to rabies.

4.4 Special warnings and precautions for use

Ensure that Rabigam IM is not administered into a blood vessel because of the risk of shock.

Repeated doses of the rabies immunoglobulin should not be administered once rabies vaccine treatment has been started, because this could prevent full development of the active immunity expected from the vaccine.

Intramuscular injections are not advocated for persons with bleeding disorders unless special precautions are taken.

Hypersensitivity

True hypersensitivity reactions are rare.

Anaphylactic reactions may occur especially if this intramuscular preparation is given intravenously. Measures to treat anaphylaxis, including adrenaline, must be immediately available when administering **Rabigam IM**.

Persons with selective immunoglobulin A (IgA) deficiency may develop antibodies to the small amount of IgA in this preparation, leading to sensitisation and subsequent reaction to IgA-containing material. The risk-benefit ratio in patients with a history of IgA deficiency or severe anaphylactic reactions to plasma products should be considered.

Transmissible agents

Standard measures to prevent infections resulting from the use of medicines prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. Despite this, when medicines prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens. Consideration should be given to appropriate vaccination of patients receiving human blood or plasma-derived medicines on a routine basis.

The measures taken are considered effective for enveloped viruses such as HIV, HBV and HCV. The measures taken may be of limited value against non-enveloped viruses such as HAV and parvovirus B19.

There is reassuring clinical experience regarding the lack of hepatitis A or parvovirus B19 transmission with immunoglobulins and it is also assumed that the antibody content makes an important contribution to viral safety.

Traceability

It is strongly recommended that when **Rabigam IM** is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

4.5 Interaction with other medicines and other forms of interactions

Live attenuated virus vaccines

Immunoglobulin administration may interfere with the development of an immune response to live attenuated virus vaccines such as rubella, mumps and varicella for a period of up to 3 months. After administration of this product, an interval of at least 3 months should elapse before vaccination with live attenuated virus vaccines. In the case of measles, this impairment may persist for up to 4 months.

Interference with serological testing

After injection of immunoglobulin, the transitory rise of the various passively transferred antibodies in the patient's blood may result in misleading positive results in serological testing.

4.6 Fertility, pregnancy and lactation

Pregnancy and breastfeeding

The safety of this medicine in pregnancy and lactation has not been established in controlled clinical trials. Clinical experience with immunoglobulins suggests that no harmful effects on the course of pregnancy, or on the foetus and the neonate are to be expected.

Fertility

No data are available.

4.7 Effects on ability to drive and use machines

Rabigam IM may cause dizziness and other side effects. Patients who experience adverse reactions during treatment should wait for these to resolve before driving or operating machines.

4.8 Undesirable effects

Summary of the safety profile

Adverse reactions such as chills, headache, dizziness, nausea, flushing, pyrexia, back pain and local reactions may occur occasionally.

List of adverse reactions

MedDRA Standard System Organ Class	Undesirable effects	Frequency
Nervous system disorders	Headache	Unknown
	Dizziness	Unknown
Vascular disorders	Flushing	Unknown
Gastrointestinal disorders	Nausea	Unknown
Skin & subcutaneous tissue disorders	Skin reactions	Unknown
Musculoskeletal and connective tissue disorder	Back pain	Unknown
General disorders and administration site conditions	Chills	Unknown
	Pyrexia	Unknown
	Injection site pain Administration site reaction	Unknown

Transmissible agents

For safety information with respect to transmissible agents, see section 4.4.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are requested to report any suspected adverse reactions to SAHPRA via the Med safety APP (Medsafety X SAHPRA) and eReporting platform (https://primaryreporting.who-umc.org/ZA) found on SAHPRA website or to National Bioproducts Institute via the email address Pharmacovigilance@nbisa.org.za.

4.9 Overdose

Consequences of an overdose are not known.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: immune sera and immunoglobulins: Human rabies immunoglobulin, ATC code: J06BB05

Category and class: A. 30.1 Biologicals (Antibodies).

Rabies immunoglobulin confers passive immunity against rabies. The pharmacodynamics effects *in vivo* of the specific neutralising antibodies against the rabies virus are not fully documented, but rabies immunoglobulin has been proven to be effective in preventing the rabies infection.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycine

Sodium chloride

Sodium hydroxide (for pH-adjustment)

Hydrochloric acid (for pH-adjustment)

Human albumin

Human hepatitis B immunoglobulin

Human normal immunoglobulin

Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 Shelf life

3 years.

From a microbiological point of view, the product should be used immediately after opening. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6.4 Special precautions for storage

Transport within 72 hours below 37 °C.

Store in a refrigerator between 2 °C and 8 °C.

Keep the ampoule in the outer carton until required for use.

Do not freeze.

Protect from light.

For in-use storage conditions, see section 6.3.

6.5 Nature and contents of container

Rabigam IM is presented as a single dose, and packaged in a 2 ml clear and colourless, type I glass, ampoule marked with an orange ring.

6.6 Special precautions for disposal and other handling

Warm the ampoule to body temperature before injecting intramuscularly.

The solution is a clear, slightly opalescent liquid, which is almost colourless or pale-yellow to light brown.

During storage, it may show formation of slight turbidity or a small amount of particulate matter.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

NATIONAL BIOPRODUCTS INSTITUTE NPC

Company Reg. No. 1994/002044/08

NPO Reg. No. 020-898-NPO

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8 REGISTRATION NUMBERS

T/30.2/748

Namibia	S2
Reg. No.:	04/30.2/1048

9 DATE OF FIRST AUTHORISATION

Registration date: 09 June 1997

10 DATE OF REVISION OF THE TEXT