Proposed Professional Information

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

Hebagam® IM, 200 IU (100 IU/ml), solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Human hepatitis B immunoglobulin.

Each 2 ml ampoule contains 200 IU (100 IU/ml) of hepatitis B antibodies.

Hebagam IM contains immunoglobulin derived from pooled human plasma, sourced from healthy donors, with a high titre of antibodies to the hepatitis B surface antigen (HBsAg).

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

Hebagam 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 **Hebagam IM**.

This preparation does not contain any antimicrobial preservatives.

Hebagam 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.

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

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Hebagam IM is used for immunoprophylaxis of hepatitis B:

- In case of accidental exposure, e.g. skin pricks, spillage into eye or mouth, bites or scratches, contamination of abrasions, in non-immunised subjects (including persons whose vaccination is incomplete or status unknown).
- In the newborn of a hepatitis B virus carrier-mother.
- In persons who have been in sexual or intimate physical contact with HBsAg-positive persons.
- In haemodialysed patients, until vaccination has become effective.
- In subjects who did not show an immune response (no measurable hepatitis B antibodies or < 10 IU/L of hepatitis B antibodies) after vaccination and for whom a continuous prevention is necessary due to the continuous risk of being infected with hepatitis B.

4.2 Posology and method of administration

Posology

INDICATIONS	SINGLE DOSE	SPECIAL INSTRUCTIONS
Needle-stick injury Mucosal exposure Sexual exposure	Age: 10 years to adult : 500 IU Age 5 - 9 years (inclusive): 300 IU Age 0 - 4 years (inclusive) : 200 IU	Treat preferably within 48 hours, and not more than 7 days after exposure. Repeat after 28 days unless recipient has been shown to be immune or has received hepatitis B vaccine.
Haemodialysis	8 - 12 IU/kg (Maximum 500 IU)	**Hebagam IM** administration may need to be repeated every 2 months until seroconversion following vaccination.
Newborn babies born to HBsAg positive mothers (especially those who are hepatitis B envelope antigen (HBeAg) positive)	200 IU	Treat preferably at birth, or within 48 hours after birth. First dose of hepatitis B vaccine must be administered at the same time. **Hebagam IM** administration may need to be repeated until seroconversion following vaccination.
In subjects who do not show an immune response after vaccination and for whom continuous prevention is necessary	Adults: 500 IU Children: 8 IU/kg	Every 2 months (a minimum protective antibody titre is considered to be 10 IU/L)

In all of the above situations, vaccination against hepatitis B virus is highly recommended. The first dose can be injected on the same day as human hepatitis B immunoglobulin, however at different sites.

Method of administration

Intramuscular route.

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.

When simultaneous vaccination is necessary, the immunoglobulin and the vaccine should be administered at two different sites to avoid interference with the active antibody response.

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

4.3 Contraindications

- Hypersensitivity to the active substance (human hepatitis B immunoglobulin) or to any of the excipients listed in section 6.1.
- Hypersensitivity to human immunoglobulins.

4.4 Special warnings and precautions for use

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

Hebagam IM is not appropriate for the treatment of any type of hepatitis B infection.

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 **Hebagam 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 **Hebagam 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.

Hebagam IM is not routinely recommended for persons at continued risk of hepatitis B infection – such as laboratory personnel, chronic dialysis patients, travelers to endemic areas and institutionalised patients – where active immunization with hepatitis B vaccine is preferable.

4.5 Interaction with other medicines and other forms of interaction

Live attenuated virus vaccines

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

Human hepatitis B immunoglobulin should be administered three to four weeks after vaccination with such a live attenuated vaccine; in case administration of human hepatitis B immunoglobulin is essential within three to four weeks after vaccination, then revaccination should be performed three months after the administration of **Hebagam IM.**

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 intramuscular immunoglobulin 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

Hebagam 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. Health care 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: Hepatitis B immunoglobulin, ATC code: J06BB04.

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

Hepatitis B immunoglobulin confers passive immunity against hepatitis B virus.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycine

Sodium chloride

Sodium hydroxide (for pH-adjustment)

Hydrochloric acid (for pH-adjustment)

Human albumin

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

Hebagam IM is presented as a single dose and packaged in a 2 ml clear and colourless, type I glass ampoule marked with a yellow 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

Private Bag X9043	10 Eden Road
Pinetown	Pinetown

3600
KwaZulu-Natal
South Africa

3610
KwaZulu-Natal
South Africa

Telephone: +27 (0) 860162472

Email: MedInfo@nbisa.org.za

8 REGISTRATION NUMBERS

T/30.2/0746

Namibia	S2
Reg. No.:	04/30.2/1144

9 DATE OF FIRST AUTHORISATION

Registration date: 16 February 1998

10 DATE OF REVISION OF THE TEXT