PACKAGE LEAFLET: INFORMATION FOR THE USER

IMMUNOHBS 180 IU/ml solution for injection for intramuscular use

Human hepatitis B immunoglobulin

Read all of this leaflet carefully before you start using this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT IMMUNOHBs IS AND WHAT IT IS USED FOR

IMMUNOHBs is a solution of human hepatitis B immunoglobulins. The immunoglobulins are blood protein and they constitute the antibodies.

IMMUNOHBs is used in the following cases:

- in order to prevent recurrence of hepatitis B virus infection after liver transplantation for liver failure caused by hepatitis B virus.
- in order to give rapidly available antibodies against hepatitis B virus to prevent hepatitis B in the following cases:
    - in case of accidental exposure in non-immunised subjects (that is persons who have not been vaccinated against the hepatitis B virus; including persons whose vaccination is incomplete or status unknown).
    - in haemodialysed patients (that is patients with a severe renal failure that need a blood purification by an artificial kidney), until vaccination has become effective
    - in the newborn of a hepatitis B virus carrier-mother.
    - in subjects who did not show an immune response after vaccination (that is persons in which the vaccination did not become effective) and for whom a continuous prevention is necessary due to the continuous risk of being infected with hepatitis B virus.

2. BEFORE YOU USE IMMUNOHBs

Do not use IMMUNOHBs

If you are allergic (hypersensitive) to human immunoglobulins or to any of the other ingredients of IMMUNOHBs.

For example, if you have a deficiency of immunoglobulin A (IgA), you may develop, in the blood, antibodies against the immunoglobulin A. IMMUNOHBs contains small quantity of IgA and therefore severe allergic reactions could occur.

The physician must therefore weigh the benefit of treatment with IMMUNOHBs against the potential risk of allergic reactions.

Take special care with IMMUNOHBs

Who administers IMMUNOHBs to you should ensure that the product is not administered into a blood vessel, this could cause an acute (o severe) crisis of the circulatory system, known as shock?

If you are a carrier of HBsAg, there is no benefit in administering this product. Serious allergic reactions are rare.

Rarely, the human anti-hepatitis B immunoglobulins can induce a sudden fall in blood pressure with disorder of breathing, faints, sometimes fever and skin reactions (anaphylactic reaction). This can happen even if you have tolerated previous treatments with immunoglobulins.

If your doctor or who administers to you the product should suspect an allergic or anaphilactic reaction must stop immediately the administration. In case of shock, your doctor should follow the standard medical treatment for shock.

The product contains 3.9 mg sodium per ml. This must be taken into consideration, depending on the total amount of product that you must assume, if you are on a low salt diet.

When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include:

- a careful selection of blood and plasma donors to make sure that those at risk of carrying infections are excluded;
- the testing of the donations to ensure that there are no infective agents and/or viruses;
- the inclusion, during manufacturing process of steps capable of inactivating or removing viruses.

Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging infectious agents or other types of infections.

The measures taken are considered effective for viruses such as human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV) and for hepatitis A virus (HAV).

The measures taken may be of limited value against viruses such as parvovirus B19. Immunoglobulins have not been associated with hepatitis A or parvovirus B19 infections possibly because the antibodies against these infections, which are contained in the product, are protective.

It is strongly recommended that every time you receive a dose of IMMUNOHBs the name and batch number of the product are recorded in order to maintain a record of the batches used.

Effects on Blood tests

If you are going to have a blood test following an administration of IMMUNOHBs, tell the nurse or the doctor that you have been administered this product.

IMMUNOHBs may interfere with some tests for red cell antibodies.

Pediatric population

No specific measures or monitoring are required for the pediatric population.

Using other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

IMMUNOHBS must not be mixed with other medicinal products.

Live attenuated virus vaccines

IMMUNOHBS may interfere with the development of an immune response to live attenuated virus vaccines such as rubella, mumps, measles and varicella. Immunoglobulin administration may interfere with the efficacy of these vaccines for a period of at least 3 months. After administration of IMMUNOHBS, at least 3 months should elapse before vaccination with live attenuated virus vaccines. Following vaccination with live attenuated virus vaccines, a period of 3 or 4 weeks should elapse before administrating human hepatitis B immunoglobulin. In case administration of human

hepatitis B immunoglobulin is required before, then revaccination should be performed three months after the administration of human hepatitis B immunoglobulin.

Pregnancy, breastfeeding and fertility

Ask your doctor or pharmacist for advice before taking any medicine.

Pregnancy

The safety of this medicinal product for use in human pregnancy has not been established in controlled clinical trials and therefore should only be given with caution to pregnant women and breast-feeding mothers. Clinical experience with immunoglobulins suggests that no harmful effects on the course of pregnancy, or on the fetus and the neonate are to be expected.

Breastfeeding

Immunoglobulins are excreted into the milk and may contribute to the transfer of protective antibodies to the neonate.

Fertility

Clinical experience with immunoglobulins suggests that no harmful effects on fertility are to be expected.

Driving and using machines

No effects on ability to drive and use machines have been observed.

3. HOW TO USE IMMUNOHBs

IMMUNOHBS should be administered by intramuscular route.

The product should be brought to room or body temperature before use.

Remove the central protection from the rubber stopper and draw the solution with an injection syringe. Change the needle and inject.

Once the solution is withdrawn from the container into the syringe, the medicinal product must be administered immediately.

The liquid preparation is clear and colorless or pale-yellow or light brown. Do not use solutions that are cloudy or have deposits.

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

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

Dose

The physician will establish which is the appropriate dose for you. The usual dose is the following:

In order to prevent recurrence of hepatitis B virus infection after liver transplantation for liver failure caused by hepatitis B virus:

In adults

The suggested posology is 2000 IU IM every 15 days in the period after the transplantation, excluding the first week. This posology should be modified in the long-term treatment to ensure the maintenance of the serous level of HBsAg antibodies above 100 IU/l in HBV-DNA negative patients and above 500 IU/l in HBV-DNA positive patients.

The concomitant use of adequate virostatic agents should be considered, if appropriate, as a standard in hepatitis B re-infection prophylaxis.

Pediatric population

There is no relevant use of UMAN BIG in the pediatric population in the indication prevention of hepatitis B virus recurrence after liver transplantation for hepatitis B induced liver failure.

In order to prevent hepatitis B:

Prevention of hepatitis B in case of accidental exposure in non-immunised subjects:

at least 500 IU (International Units), depending on the intensity of exposure, as soon as possible after exposure, and preferably within 24 - 72 hours.

Immunoprophylaxis of hepatitis B in haemodialysed patients:

8-12 IU/kg with a maximum of 500 IU, every 2 months until the vaccination has become effective Prevention of hepatitis B in the newborn, of a hepatitis B virus carrier-mother, at birth or as soon as possible after birth:

30-100 IU/kg. The hepatitis B immunoglobulin administration may need to be repeated until the vaccination has become effective.

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

If you have not shown an immune response after vaccination (no measurable hepatitis B antibodies), and in case a continuous prevention is necessary, the doctor may consider the administration of 500 IU (to adults) and 8 IU/kg (to children) every 2 months.

If you use more IMMUNOHBs than you should

Consequences of an overdose are not known.

4. POSSIBLE SIDE EFFECTS

Like all medicines, IMMUNOHBS can cause side effects, although not everybody gets them.

The table presented below is according to the MedDRA system organ classification (SOC and Preferred Term Level).

Frequencies have been evaluated according to the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

There are no robust data on the frequency of undesirable effects from clinical trials. The following undesirable effects have been reported:

MedDRA Standard System Organ Class	**Undesirable effects**	**Frequency**
Immune system disorders	Hypersensitivity	Not known
	Anaphylactic shock	Not known
Nervous system disorders	Headache	Not known
Cardiac disorders	Tachycardia	Not known
Vascular disorders	Hypotension	Not known
Gastrointestinal disorders	Nausea	Not known
	Vomiting	Very rare
Skin and subcutaneous tissue disorders	Skin reaction	Not known
	Erythema	Not known
	Itching	Not known
	Pruritus	Not known
Musculoskeletal and connective tissue disorders	Arthralgia	Not known
	Fever,	Not known
	Malaise,	Not known
	Chill	Not known

General disorders and administration site conditions	At injection site: pain	Uncommon
	At injection site: swelling, erythema, induration, warmth, pruritus, rash, itching	Not known

For information on safety with respect to transmissible agents, see the section "2. Before you use IMMUNOHBS".

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

Pediatric population

Frequency, type and severity of adverse reactions in children are expected to be the same as in adults.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [To be completed with the national reporting system listed in Appendix V]. By reporting side affects you can help provide more information on the safety of this medicine.

5. HOW TO STORE IMMUNOHBs

Store in a refrigerator (2ºC / 8ºC).

Keep in the outer carton in order to protect from light.

Keep out of the reach and sight of children.

Do not use IMMUNOHBS if you notice the solution is cloudy or has deposits (see also "What IMMUNOHBS looks like" at point 6. "FURTHER INFORMATION").

Do not use IMMUNOHBS after the expiry date which is stated on the carton and on the label. Medicines should not be disposed of via wastewater or household waste.

Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What IMMUNOHBS contains

The active substance is human hepatitis B immunoglobulin.

	IMMUNOHBS 180 IU/1 ml	**IMMUNOHBS 540 IU/ 3 ml**
Human proteins	100-180 g/l	100-180 g/l
of which human immunoglobulin at least	90%	90%
antibodies to HBs antigen (anti - HBs) not less than	180 IU/ml 180 IU/vial	180 IU/ml 540 IU/vial

Distribution of IgG subclasses:

IgG1 63.7 %
IgG2 31.8 %
IgG3 3.3 %
IgG4 1.2 %

The maximum content of IgA is 03 mg /ml.

The other ingredients are glycine, sodium chloride, water for injections.

What IMMUNOHBS looks like and contents of the pack

IMMUNOHBS is a solution for injection.

The color can vary from colorless to pale-yellow up to light brown; during storage it may show formation of slight turbidity or a small amount of particulate matter.

IMMUNOHBS 180 IU solution for injection: vial with 180 IU in 1 ml

Marketing Authorization Holder

Kedrion S.p.A. - Loc. Ai Conti, 55051 Castelvecchio Pascoli, Barga (Lucca) Italy.

Manufacturer

Kedrion S.p.A. - S.S. 7 bis Km 19,5, S. Antimo (Napoli), Italy.

This medicinal product is authorized in the Member States of the EEA under the following names:

Austria	IMMUNOHBS 180 I.E./ml Injektionslösung
Denmark	IMMUNOHBs
Germany	IMMUNOHBS
Hungary	Umanbig 180 NE/ml oldatos injekció
Italy	IMMUNOHBS
Poland	IMMUNOHBS
Portugal	IMMUNOHBs
Sweden	Umanbig

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