على كلا من التركيز (180 IU/ml و 540 IU/3ml) ولا تسري على تركيز 1000 IU/3ml.

Package Leaflet: Information for the user

IMMUNOHBs 180 IU/ml Solution for injection
IMMUNOHBs 540 IU/3ml Solution for injection
IMMUNOHBs 1000 IU/3ml Solution for injection

Human hepatitis B immunoglobulin

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any of the side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What IMMUNOHBs is and what it is used for

IMMUNOHBs is a solution of human hepatitis B immunoglobulins which are the antibodies against the hepatitis B virus.
IMMUNOHBs is used in the following cases:

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

2. What you need to know before you use IMMUNOHBs

Do not use IMMUNOHBs

- If you are allergic to human immunoglobulins or any of the other ingredients of this medicine (listed in section 6).

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3. How to use IMMUNOHBs

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

IMMUNOHBs should be administered via the intramuscular route.
The product should be brought to room or body temperature before use.

Vials: 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.
Pre-filled syringe : screw in the plunger shaft and inject.
Attention: the injection must be carried out after having ensured that a blood vessel has not been penetrated.

The solution is clear and colourless or pale-yellow or light-brown. Do not use solutions which 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 it in divided doses at different sites.
Moreover, if you suffer from thrombocytopenia and other disorders of haemostasis, IMMUNOBHs must not be administered intramuscularly.

Dose
The physician will establish which is the appropriate dose for you.
The usual dose is the following:
In order to prevent the recurrence of hepatitis B virus infection after liver transplantation due to liver failure caused by hepatitis B virus:

Adults
2000 IU every 15 days.
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. 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 standard of hepatitis B re-infection prophylaxis.

Use in children
No data are available regarding the use of IMMUNOHBs in the pediatric population for the indication prevention of hepatitis B virus recurrence after liver transplantation for hepatitis B induced liver failure.

In order to prevent hepatitis B in the following cases:

Prevention of hepatitis B in case of accidental exposure in non-immunised subjects:
at least 500 IU, 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 vaccination has become effective.

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.

Children
No specific measures or monitoring are required for the paediatric population.

Other medicines and IMMUNOHBs
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
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, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this 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. 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.

Breast-feeding
The safety of IMMUNOHBs for use in breast-feeding mothers has not been established in controlled clinical trials and therefore it must only be given with caution to breast-feeding women.
Immunoglobulins are excreted into the milk and may contribute to protecting the neonate from pathogens which have a mucosal portal of entry.

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

Driving and using machines
IMMUNOHBs has no or negligible influence on the ability to drive and use machines have been observed. Patients who experience adverse reactions during treatment should wait for these to resolve before driving or operating machines.

IMMUNOHBs contains sodium
This medicinal product contains up to 3.9 mg per 1 ml vial and 11.7 mg sodium per 3 ml vial (sodium is the main component of cooking/table salt).
This is equivalent to 0.19% and 0.58% of the recommended maximum daily dietary intake of sodium for an adult.

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- If you have a deficiency of immunoglobulin A (IgA), you may develop antibodies against the immunoglobulin A in the blood. IMMUONOHBs 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.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using IMMUNOHBs

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

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

Hypersensitivity
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 anaphylactic reaction, the administration must immediately be stopped. In case of shock, your doctor should follow the standard medical treatment for shock.

If you notice any of these symptoms: difficulty breathing, pain and swelling of a limb, loss of movement or sensitivity in a part of the body (focal neurological deficits) and chest pain, ask your doctor immediately or contact the nearest hospital, because you could be have an ongoing thrombotic event.

When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients.
These measures 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 transmitting infective agents 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 enveloped viruses such as the human immunodeficiency virus (HIV), hepatitis B virus (HBV) hepatitis C virus (HCV) and for the non-enveloped hepatits A virus (HAV).
The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19.

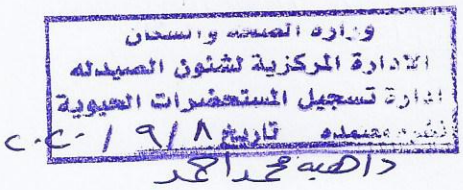
Immunoglobulins have not been associated with hepatitis A or parvovirus B19 infections possibly because the antibodies against these infections, which are contained in the product, are protective.

It is strongly recommended that every time you receive a dose IMMUNOHBs, 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.

<u>Effects on Blood tests</u>

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 did not show an immune response after vaccination (no measurable hepatitis B antibodies), and in case continuous prevention is necessary, your doctor can consider 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, this medicine can cause side effects, although not everybody gets them.

If you notice any of these side effects, ask your doctor immediately or contact the nearest hospital:

- Allergic reaction (hypersensitivity), anaphylactic shock (an extreme, often life-threatening allergic reaction). Symptoms of allergic reaction/anaphylactic shock include for example pruritus, skin reactions, swelling of the lips, face, and tongue, difficulty swallowing, trouble in breathing, fainting.

The following side effects may generally occur after treatment with human immunoglobulins administered intramuscularly:
- adverse reactions as chills, headache, dizziness, fever, vomiting, allergic reactions, nausea, arthralgia (joint pains), low blood pressure and moderate low back pain may occur occasionally;
- rarely human normal immunoglobulins may cause a sudden fall in blood pressure (hypotension) and, in isolated cases, hypersensitivity reactions (anaphylactic shock), even when the patient has shown no hypersensitivity to previous administration.
- local reactions at injection site: soreness, swelling, redness (erythema), induration, local heat, pruritus, rash, itching, may frequently occur.

The following side effects have been reported following administration of IMMUNOHBs during marketed use of the medicinal product (the frequency cannot be estimated from available data):

- Headache
- Accelerated heartbeat (Tachycardia)
- Fall in blood pressure (Hypotension)
- Nausea
- Vomiting
- Skin reaction, redness (erythema), itching, pruritus
- Joint pain (Arthralgia)
- Fever
- Malaise
- Chills
- At injection site: pain, swelling, erythema, induration, warmth, pruritus, rash, itching

For information on safety with respect to transmissible agents, see the section 2 *"What you need to know before you use IMMUNOHBs"*.

Additional side effects in children

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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store IMMUNOHBs

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the outer carton and on the label.
The expiry date refers to the last day of that month.
Store in a refrigerator (2°C - 8°C).
Keep in the outer carton in order to protect from light.
Do not freeze.
Do not use this medicine if you notice the solution is cloudy or has deposits (see also *"What IMMUNOHBs looks like and content of the pack"* at section 6).
Do not throw away any medicines via wastewater or household waste.
Ask your pharmacist how to dispose of medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What IMMUNOHBs contains
The active substance is human hepatitis B immunoglobulin.

	IMMUNOHBs 180 IU/ml IMMUNOHBs 540 IU/3ml	IMMUNOHBs 1000 IU/3 ml
Human proteins	100-180 g/l	100-180 g/l
of which human immunoglobulin (IgG) at least to	90%	90%
antibodies to HBs antigen (anti-HBs) not less than	180 IU/ml (180 IU in 1 ml vial) (540 IU in 3 ml vial)	334 IU/ml (1000 IU in 3 ml pre-filled syringe)

Distribution of IgG subclasses:
IgG_1 63.7 %
IgG_2 31.8 %
IgG_3 3.3 %
IgG_4 1.2 %

The maximum content of IgA is 300 micrograms/ml.
Produced from the plasma of human donors.

The excipients are glycine, sodium chloride, water for injections.

What IMMUNOHBs looks like and contents of the pack
IMMUNOHBs is a solution for injection.

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The colour can vary from colourless 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
IMMUNOHBs 180 IU solution for injection: vial with 540 IU in 3 ml
IMMUNOHBs 334 IU solution for injection: pre-filled syringe with 1000 IU in 3 ml

Marketing Authorisation Holder and Manufaturer
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).

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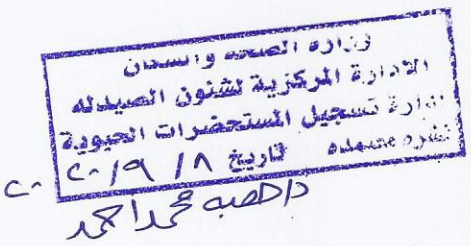

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