PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only.

Zutectra 500 IU, Solution for Injection

One pre-filled syringe of 1 mL contains the active ingredient: Human hepatitis B immunoglobulin 500 IU/mL.

Zutectra contains 150 mg/mL of a human plasma protein, of which at least 96% is immunoglobulin G (IgG). The maximum immunoglobulin A (IgA) content is 6,000 micrograms/mL.

For the list of inactive ingredients, please see section 6.

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed to treat your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

This medicine is intended for adults only.

- Zutectra contains antibodies against the hepatitis B virus, which are the body's own defensive substances to protect you from hepatitis B. Hepatitis B is an inflammation of the liver caused by the hepatitis B virus.
- **Information on the starting material of Zutectra and the possibility of transmission of infectious agents:**
  Since this product is made from human plasma, there is a possibility of transmission of infectious agents, such as viruses or other types of infections.
  It is important to keep a record of the name and batch number of your Zutectra. So, every time you get a new package of Zutectra, **note down the date and the batch number** (which is on the packaging after "Lot") and keep this information in a safe place, for example your treatment diary (see section 3).
- **Vaccinations:**
  Zutectra can reduce the effectiveness of some vaccines (measles, rubella, mumps, chickenpox) for a period of up to 3 months.
  You may have to wait at least 3 months after the last injection of Zutectra before you can have live attenuated vaccines.
  Please tell your doctor about your treatment with Zutectra prior to any vaccination.

1. WHAT IS THE MEDICINE INTENDED FOR?

Zutectra is intended to prevent re-infection of hepatitis B in adults who have had a liver transplant at least 1 week ago, due to liver failure caused by hepatitis B.

Therapeutic group: Hepatitis B immunoglobulin.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- **You are allergic to the active ingredient (human immunoglobulins) or to any of the other ingredients of this medicine** (listed in section 6). In particular, in very rare cases of insufficient amount of immunoglobulin A (IgA), when you have antibodies against IgA in your blood. This might lead to severe allergic reaction (anaphylaxis).
  An allergic reaction may include sudden wheezing, difficulty in breathing, fast pulse, swelling of the eyelids, face, lips, throat, or tongue, rash or itching.

Special warnings regarding use of the medicine

- **Prior to treatment with Zutectra, inform the doctor** about any medicine or food to which you are sensitive to.
- **Zutectra is for subcutaneous (under the skin) injection only.** Injection into a vein or blood vessel may result in allergic shock.
- **Please tell your doctor or healthcare professional prior to treatment if** you have been told that you have antibodies against immunoglobulins of the IgA type in your blood. This is a very rare condition which may result in allergic reaction.
- **You may be allergic to immunoglobulins** (antibodies) without knowing it, even if you have tolerated previous treatments with human immunoglobulins. Particularly if you do not have enough immunoglobulins of the type IgA in your blood, allergic reactions such as a sudden fall in blood pressure or shock may occur.
- **You will be carefully observed during and shortly after the first injection of Zutectra** to make sure that you do not suffer from a reaction. If you have an allergic reaction to Zutectra, the injection will be stopped immediately. Please tell your doctor or healthcare professional immediately if you notice any reaction during your injection with Zutectra.
- **If you are HBs antigen positive,** you will not receive Zutectra, since there is no benefit in administering this medicine to you. Your doctor will be able to explain this to you.
- **For your own safety,** you will be monitored for antibody levels regularly.
- **Possible interference with blood tests:** Zutectra might affect the results of certain blood tests (serological tests). Please tell your doctor about your treatment with Zutectra prior to any blood test.

Information on the starting material of Zutectra and the possibility of transmission of infectious agents:
Zutectra is made from human plasma. Since this product is made from human plasma, there is a possibility of transmission of infectious agents, such as viruses or other types of infections.
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:
Careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded, and the testing of each donation and pools of plasma for signs of virus/infections.
Manufacturers of these medicines also include steps in the processing of the blood or plasma that can remove or inactivate 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 viruses or other types of infections.
The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the non-enveloped hepatitis A virus.
The measures taken are not considered effective against infections caused by parvovirus B19 virus, although apparently the antibodies in the product have protective effect against infections by this virus.

It is important to keep a record of the name and batch number of your Zutectra. So, every time you get a new package of Zutectra, **note down the date and the batch number** (which is on the packaging after "Lot") and keep this information in a safe place, for example your treatment diary (see section 3).

If you are taking, or have recently taken, or if you plan to take, other medicines, including non-prescription medicines and nutritional supplements, inform the doctor or pharmacist.
Zutectra can reduce the effectiveness of some vaccines (measles, rubella, mumps, chickenpox) for a period of up to 3 months.
You may have to wait at least 3 months after the last injection of Zutectra before you can have live attenuated vaccines.
Please tell your doctor about your treatment with Zutectra prior to any vaccination.

Pregnancy, breastfeeding and fertility: If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or healthcare professional for advice before taking this medicine.

Driving and using machines: Zutectra has no or negligible effects on your ability to drive or use machines.

3. HOW SHOULD YOU USE THE MEDICINE?

- Always use according to the doctor's instructions.
- Check with the doctor or pharmacist if you are uncertain.
- **Zutectra is intended for subcutaneous (under the skin) injection.** The content of one pre-filled syringe is intended for use once only. **Do not inject into a blood vessel.**
- In most cases, you will be given the injection by your doctor or nurse. However, if your antibody levels are sufficient and you have a fixed dose regimen, you or your caregiver may be trained to carry out the injections at home (see below).
- For the documentation of your injections of Zutectra it is strongly recommended to use the treatment diary. Your doctor will explain you how to use it.
- **The dosage and treatment regimen will be determined by the doctor only.**
- **Do not exceed the recommended dose.**
- Do not swallow.
- The dose will depend on your condition. Your doctor will regularly check your condition and tell you how much and how often you need to use Zutectra.
- **Injecting by yourself or by a caregiver:**
  You can inject Zutectra yourself without the help of your doctor, if they have trained you to do this. **If you are administering Zutectra yourself, please read the instructions in the section "How to inject Zutectra by yourself or by a caregiver" carefully.**
  Zutectra must be brought to room temperature (approx. 23°C-27°C) before use.

Tests and follow-up: Before commencing treatment with the medicine, and during the course of treatment, you will be monitored for antibody blood levels regularly.

- **If you accidentally took a higher dosage,** contact your doctor, healthcare professional or pharmacist straight away for advice. Consequences of an overdose are not known.
- If you took an overdose or if a child accidentally swallowed the medicine, immediately refer to a doctor or proceed to a hospital emergency room and bring the package of this medicine with you.
- **If you have forgotten to take this medicine** at the specified time, do not take a double dose. Consult the doctor about managing the dose. Your doctor will explain to you how much and how often you need to use Zutectra.
- **Make sure you use Zutectra as prescribed and as instructed by the doctor, to avoid the risk of hepatitis B re-infection.**
- Even if there is an improvement in your health, do not discontinue treatment with the medicine without consulting the doctor.
- **Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.**
- **If you have further questions regarding use of this medicine, consult a doctor or pharmacist.**

4. SIDE EFFECTS

As with any medicine, use of Zutectra may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.
In very rare cases human normal immunoglobulins may cause a serious allergic reaction.

Discontinue use and refer to a doctor immediately if you notice any of the following effects: rash, itching, wheezing, difficulty in breathing, swelling of the eyelids, face, lips, throat or tongue, low blood pressure or fast pulse.
This can be an allergic reaction or a serious allergic reaction (anaphylactic shock).
In case of any adverse event after the injection, speak to your doctor immediately.

Additional side effects that have been reported during use of Zutectra

Common (may affect up to 1 in 10 people): injection-site reactions: pain, hives (urticaria) at injection site, haematoma (a collection of blood in tissue under the skin), reddening of the skin (erythema).

Uncommon (may affect up to 1 in 100 people): headache, upper abdominal pain (from your chest to the belly button).

Furthermore, the following reactions have been reported once only: tiredness (fatigue), high blood pressure (hypertension), inflammation of the nose and throat (nasopharyngitis), muscle spasm, allergic reactions (hypersensitivity), abnormal heartbeat (palpitations), cardiac discomfort, itching (pruritus), rash, pain in the mouth and throat.

With other human immunoglobulin preparations, the following additional symptoms have been reported: chills, headache, dizziness, fever, vomiting, mild allergic reactions, nausea (urge to vomit), joint pain, low blood pressure, moderate low back pain, injection-site reactions: swelling, soreness, redness, hardening of the skin, local heat, itching, bruising and rash.

If you get any side effect, if any of the side effects gets serious or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.

Reporting of suspected adverse reactions
Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il
Additionally, you may also report to Kamada Ltd. to the email address: pharmacovigilance@kamada.com

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without explicit instruction from the doctor.
- Do not use the medicine after the expiry date (Exp. Date) which is stated on the outer carton package, the blister and the pre-filled syringe label. The expiry date refers to the last day of that month.
- Store and transport refrigerated (2°C-8°C).
- Do not freeze.
- Store the pre-filled syringe in the original package in order to protect from light.
- Once the protective cap has been removed from the pre-filled syringe, the solution should be administered immediately.
- Do not use Zutectra if you notice that the solution is cloudy or contains particles.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.
  Once the injection has been completed, dispose of all needles, syringes and empty glass containers without delay in a container intended for sharp objects.

6. FURTHER INFORMATION

- In addition to the active ingredient, the medicine also contains:
  Glycine and water for injections.
- What the medicine looks like and the contents of the pack:
  Zutectra is provided as a solution for injection in a pre-filled syringe (one 1 mL pre-filled Zutectra syringe contains 500 IU). Zutectra comes in a package containing 5 pre-filled syringes, in a blister package.
  The color of the solution is clear to opalescent and colourless to pale yellow.
- License holder: Kamada Ltd., Beit Kama.
- Manufacturer: Biotest Pharma GmbH, Germany.
- Revised in April 2022 according to the MOHs guidelines.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 1502633639.

How to inject Zutectra by yourself or by a caregiver

The following instructions are intended to explain how to inject Zutectra. Please read the instructions carefully and follow them step by step. The doctor or healthcare professional will teach you the process of administration.
Do not attempt to inject Zutectra until you are sure that you understand how to prepare the injection solution and give the injection.

General information:

- Keep the syringes and syringe disposal unit out of the reach of children; lock the supplies if possible.
- Try to take the injection at the same time of day. This makes it easier to remember it.
- Always double check the dose.
- The solution must be brought to room temperature (approx. 23°C-27°C) before use.
- Take each pre-filled syringe only out of the pack when you are ready for an injection. Once the protective cap has been removed from the pre-filled syringe, you should administer the injection immediately.
- The color of the solution can vary from clear to opalescent and colourless to pale yellow. Do not use solutions that are cloudy or have particles.
- This medicine must not be mixed with other medicines.

Before the injection:

1. Wash your hands. It is important to have your hands and the items you use as clean as possible.
2. Lay out everything you need in advance. Find a clean place where you can spread out all the items you are going to use:
   - two alcohol swabs.
   - one pre-filled syringe of Zutectra.
   - one needle suitable for subcutaneous injection.

   Please note that the alcohol swabs and needles are not contained in the pack and you need to supply them yourself.
   Make sure to have your treatment diary and a container intended for sharp objects for waste disposal available.
3. Before preparing the injection, decide where you are going to inject. You should inject Zutectra into the fatty layer between the skin and muscle (about 8-12 mm under the skin). The best places for injections are where the skin is loose and soft, for example, in the abdomen, arm, thigh or buttocks, and away from joints, nerves and bones.
   Important: Do not use on any area where you can feel lumps, bumps, firm knots, pain or on an area that is discolored, indented, scabbed or where the skin is broken. Talk to the doctor or healthcare professional about these or any other unusual condition you may find. You should rotate the injection site at every injection, each injection in a different area of the body. If some areas are too difficult for you to reach, you may need a caregiver to help you with these injections.
4. Prepare the Zutectra pre-filled syringe:

- Take the pre-filled syringe out of the pack.
- Examine the solution carefully. It should be clear and contain no particles. If the solution is cloudy, contains particles or discolored discard it and start again with a new pre-filled syringe.
- Remove the protective cap from the syringe.

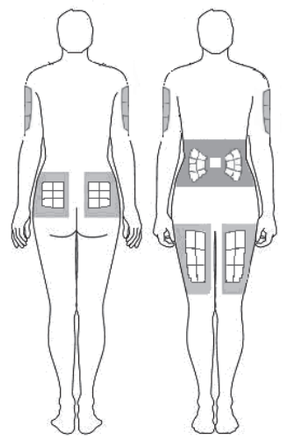
- Take the needle out of its sterile pack and fit the needle onto the syringe.

5. Get rid of any air bubbles that may be in the pre-filled syringe.

- Hold the syringe with the needle pointing upwards and tap the syringe gently with your fingers until all the air has collected at the tip. Carefully push the plunger in until the air bubbles have disappeared.

Injection:

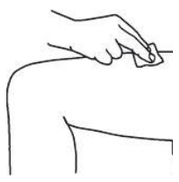
1. Choose the area where you will make the injection and make a note of it in the diary. Further, note down the date and the batch number (see "Information on the starting material of Zutectra and the possibility of transmission of infectious agents" in section 2 of this package leaflet).



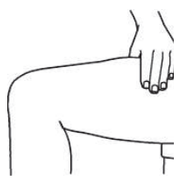
- Abdomen (stomach): Do not use the area within 2.5 cm around the navel. Avoid using the belt line area, as rubbing may irritate the injection site. Avoid surgical scars. This is likely to be the easiest place to inject if you are doing it yourself.
- Thighs: Use middle and outer areas where you can pinch up tissue. You are likely to have more fatty tissue the closer you are to the hip and the further you are from the knee.
- Arms: The back of the upper arm should be used. It is hard to pinch up the tissue and inject Zutectra yourself using this site. If you do choose to inject your arm yourself, try to pinch up the tissue by placing your upper arm over the back of a chair or brace it against a wall. It is much easier for someone else to use this site if you do need help.
- Buttocks: Use any area where you can pinch up tissue. It is harder to give yourself an injection here. Try standing in front of a mirror to locate the site or you may want to ask your caregiver to give you the injection.

It is important to change (rotate) the injection sites. This will help the skin stay supple and help the medicine be absorbed evenly. Rotating sites means starting at one site and using all other sites before going back to the first site you used. Then start the rotation again. It may be helpful to keep a record of where you had the last injection to avoid problems.

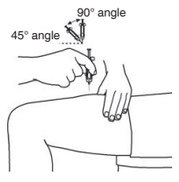
The administration in thighs is shown as an example in the following pictures:



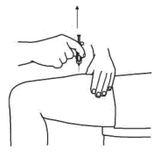
2. Wipe the intended area with an alcohol swab. Let the skin air-dry.



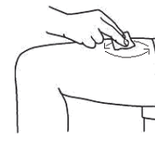
3. Gently pinch the skin together around the disinfected injection site (to raise it up a little) and push the needle into the skin with a rapid, confident movement at an angle of 45 to 90 degrees. Inject beneath the skin as you have been shown by the doctor or nurse.



4. Inject the liquid by pressing gently on the plunger. Allow yourself enough time to inject the whole of the solution, until the syringe is empty.



5. Then pull the needle out immediately and let go of the pinched skin.



6. Clean the injection site by wiping it in a circular motion with the alcohol swab.

Dispose of all used items
Once the injection has been completed, dispose of all needles and empty glass containers without delay in a container intended for sharp objects.