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

The medicine is dispensed with a doctor's prescription only

HUMIRA 40 mg

Solution for injection in a single-use vial

Active ingredient:
Each vial contains: adalimumab 40 mg/0.8 ml
Inactive ingredients and allergens - see section 6 "Further Information".

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 for you, do not pass it on to others, it may harm them, even if it seems to you that their ailment is similar.

1) WHAT IS THE MEDICINE INTENDED FOR?

Humira decreases the inflammatory process in the diseases for which the medicine is intended.
The active ingredient, adalimumab, is a human monoclonal antibody produced by cultured cells. Monoclonal antibodies are proteins that recognize and bind to other unique proteins. Adalimumab binds to a specific protein (tumor necrosis factor - TNFα), which is present at increased levels in inflammatory diseases, thereby blocking its activity and decreases the inflammation process.

Humira is intended for the treatment of:
- Rheumatoid arthritis when other accepted treatments have been inadequate.
- Severe, progressive rheumatoid arthritis in patients not previously treated with methotrexate.
- Polyarticular juvenile idiopathic arthritis in children and adolescents aged 2 to 17 years, when other accepted treatments have been inadequate.
- Severe ankylosing spondylitis when other accepted treatments have been inadequate.
- Psoriatic arthritis when other accepted treatments have been inadequate.
- Psoriasis when other accepted treatments have been inadequate.
- Severe plaque psoriasis in children and adolescents aged 4 to 17 years, when accepted topical treatment or phototherapy is either inappropriate or has been inadequate.
- Crohn's disease in children aged 6 to 17 years and adults, when other accepted treatments have been inadequate.
- Moderate to severe ulcerative colitis when other accepted treatments have been inadequate.
- Severe non-radiographic axial spondyloarthritis in adults, when there was an inadequate response or intolerance to non-steroidal anti-inflammatory drugs (NSAIDs).
- Active moderate to severe hidradenitis suppurativa in adults, when accepted treatment has been inadequate.

There is no information regarding children below 2 years of age and use of Humira.

Therapeutic group: TNF blocker.

2) BEFORE USING THE MEDICINE

☒ Do not use the medicine if:
- You are sensitive (allergic) to the active ingredient or to any of the additional ingredients included in the medicine (for a list of the inactive ingredients, see section 6 "Further Information").
- You suffer from a severe infection, including active tuberculosis (see additional details in the "Special Warnings Regarding Use of The Medicine" section). It is important to inform the doctor if you have symptoms of infection, such as: fever, wounds, feeling tired and dental problems.
- You suffer from moderate or severe heart failure. It is important to inform the doctor if you suffer, or have suffered in the past, from a severe heart condition (see additional details in the "Special Warnings Regarding Use of The Medicine" section).

Special Warnings Regarding Use of The Medicine

❗Before treatment with Humira tell the doctor or pharmacist:
- If you suffer from allergic reactions with symptoms, such as: chest tightness, wheezing, dizziness, swelling or rash, stop treatment with the medicine and refer to the doctor immediately.
- If you suffer from an infection, including long-term or localized infection (for example, leg ulcer), consult the doctor before using Humira. If you are unsure about this matter, contact the doctor.
- During the treatment with Humira, you may get infections more easily. This risk may increase if your lung function is impaired. These infections may be serious and include tuberculosis, infections caused by viruses, fungi, parasites or bacteria, or other opportunistic infections and sepsis, that may, in rare cases, be life-threatening. It is important to tell the doctor if you have symptoms, such as: fever, wounds, feeling tired or dental problems. The doctor may recommend temporary discontinuation of Humira.
- As cases of tuberculosis have been reported in patients treated with Humira, the doctor will check you for signs or symptoms of tuberculosis before starting treatment with Humira. This will include a thorough medical evaluation, including your medical history and appropriate screening tests (for example, chest X-ray and a tuberculin test). It is important that you tell the doctor if you have ever had tuberculosis, or if you have been in close contact with someone who has had tuberculosis in the past.
  Tuberculosis can develop during treatment with Humira even if you have received preventive treatment for tuberculosis. If symptoms of tuberculosis (persistent cough, weight loss, listlessness, mild fever), or of any other infection appear during or after treatment with Humira, refer to the doctor immediately.
- Advise the doctor if you reside or travel in regions where fungal infections such as: histoplasmosis, coccidioidomycosis or blastomycosis are endemic.
- Advise the doctor if you have suffered in the past from recurrent infections or other conditions that increase the risk of infection.
- Advise the doctor if you are a carrier of the hepatitis B virus (HBV), if you suffer from an active HBV or if you think you are at risk of contracting HBV. The doctor should conduct tests to check whether you are a carrier of HBV. Humira may cause "reactivation" of HBV in carriers. In some rare cases, especially if you are taking other medicines that suppress the immune system, reactivation of the virus can be life-threatening.
- If you are over 65 years, you may be more susceptible to infections while taking Humira. You should pay special attention and tell the doctor if symptoms of infection, such as: fever, wounds, feeling tired or dental problems appear.
- If you are about to undergo surgery or a dental procedure, inform the doctor that you are taking Humira. The doctor may recommend temporary discontinuation of Humira treatment.
- If you suffer from a demyelinating disease such as multiple sclerosis, the doctor will decide if you should receive Humira.
- Certain vaccines may cause infections and should not be given during treatment with Humira. Consult the doctor before you receive any vaccine. It is recommended that child patients, if possible, complete all vaccinations in accordance with current vaccination guidelines prior to initiating treatment with Humira. If you received Humira while you were pregnant, your baby may be at a higher risk for contracting an infection for up to approximately five months after the last dose you received during pregnancy. It is important that you tell your baby's doctors and other health-care professionals about the Humira treatment that you received during pregnancy so that they can decide when your baby may receive vaccinations.
- If you suffer from mild heart failure and you are being treated with Humira, your heart failure status must be closely monitored by the doctor. It is important to inform the doctor if you have had or have a serious heart condition. If you develop new or worsening symptoms of heart failure (e.g., shortness of breath or swelling of the feet), contact the doctor immediately. The doctor will decide if you should receive Humira.
- In some patients the body may fail to produce enough of the blood cells that help fight infections or stop bleeding. If you develop a fever that does not go away, bruises or bleed very easily or if you look very pale, refer to the doctor immediately. It is possible that the doctor will decide to stop treatment.
- There have been very rare cases of certain kinds of cancer in adults and children taking Humira or other TNF blockers.
  Patients with more serious rheumatoid arthritis that have had the disease for a long time may be at a higher risk than average of getting lymphoma (a kind of cancer that affects the lymph system) and leukemia (a kind of cancer that affects the blood and bone marrow).
  If you are treated with Humira, the risk of getting lymphoma, leukemia or other cancers may increase. On rare occasions, a specific and severe type of lymphoma has been observed in patients taking Humira. Some of those patients were also treated with azathioprine or 6-mercaptopurine. Tell the doctor if you are taking azathioprine or 6-mercaptopurine together with Humira.
  In addition, cases of non-melanoma skin cancer have been observed in patients taking Humira. Tell the doctor if new skin lesions appear during or after therapy with Humira or if existing lesions change appearance.
- There have been reports of cases of cancer other than lymphoma in patients with Chronic Obstructive Pulmonary Disease (COPD) treated with another TNF blocker. If you suffer from COPD, or if you are a heavy smoker, you should consult the doctor as to whether treatment with a TNF blocker is appropriate for you.

❗Treatment in children and adolescents:
Vaccinations: if possible, complete all vaccinations in accordance with current vaccination guidelines prior to initiating treatment with Humira.
Do not give Humira to patients with polyarticular juvenile idiopathic arthritis below 2 years of age.

❗If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.
- Do not take Humira with medicines containing the active ingredient anakinra or abatacept (these medicines are used to treat rheumatoid arthritis).
- Humira can be taken together with methotrexate or other medicines for treatment of arthritis (leflunomide, sulfasalazine, hydroxychloroquine and injectable gold preparations), steroids or analgesics, including non-steroidal anti-inflammatory drugs (NSAIDs).

If you have any questions, ask the doctor.

❗Use of the medicine with food and beverage
If you are sensitive to any type of food or medicine, inform the doctor before taking the medicine.
Since Humira is injected subcutaneously, food and drink do not affect the medicine.

❗Pregnancy and breastfeeding
The effects of the medicine in pregnant women are not known and so the use of Humira during pregnancy is not recommended.
It is recommended that you avoid becoming pregnant and you must use adequate contraception during treatment with Humira and for at least 5 months after the last Humira treatment.
Consult the doctor if you become pregnant during the course of treatment with Humira.
It is not known whether adalimumab, the active ingredient in Humira, passes into breast milk. Do not breastfeed during the entire period of treatment with the medicine and for at least 5 months after the last treatment.
If you received Humira during your pregnancy, your baby may be at a higher risk for getting infections. Before your baby receives any vaccinations, it is important to inform your baby's doctor and the health staff at the clinic and at the infant welfare center about your Humira treatment during pregnancy (see additional information in the "Special Warnings Regarding Use of The Medicine" section, in the paragraph that addresses vaccinations).
If you think you are pregnant or are planning to become pregnant, consult the pharmacist or doctor before taking this medicine.

❗Driving and using machines
Humira may have a minor effect on the ability to drive, cycle or operate machines.
After treatment with Humira, dizziness and vision disturbances may occur.

❗Smoking
If you are a heavy smoker, you should consult the attending doctor as to whether treatment with TNF blockers is appropriate for you (for further information see "Special Warnings Regarding Use of The Medicine" section).

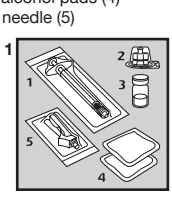
3) HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions.
Check with the doctor or pharmacist if you are uncertain.
This medicine is not intended for use in infants and children under 2 years of age.
Humira is injected under the skin (subcutaneously).
The dosage and treatment regimen will be determined by the attending doctor only.
Do not exceed the recommended dose.

Directions for using the medicine - General instructions:
The following instructions explain how to inject Humira. Please read the instructions carefully and follow them step by step. Your doctor or the nurse will teach you the technique of self-injection and the amount you should inject. Do not attempt to inject the medicine alone until you are sure that you understand how to prepare and inject the medicine. After proper training, the medicine can be self-administered or be injected by another person, for example, a parent, relative or friend.
Failure to perform the following steps can cause contamination of the medicine, which may lead to infection of the patient.
This medicine should not be mixed in the same syringe or vial with any other medicine.

1. Preparation:
- Make sure you know the proper amount (volume) needed for dosing. If you do not know the amount, **stop here** and contact the doctor for instructions.
- Make sure there is a special container to collect the syringes after use and place it on your work surface (ask the doctor/nurse for an appropriate container).
- Wash your hands thoroughly.
- Take out one inner carton from the refrigerator containing: one syringe, one vial adapter, one vial, two alcohol pads and one needle. If in the package there remains an additional inner carton for another injection, return it to the refrigerator immediately.
- Check the expiry date on the carton package and on the vial. **Do not use** the medicine and any of the items after this date.
- Make sure that the package is not damaged and that no items are missing. If the package is damaged or items are missing, do not use Humira and contact the pharmacist in the pharmacy.
- Set up the following items on a clean surface, **without taking them out of their individual transparent packages** (see picture number 1):
  - One 1 ml syringe (1)
  - One vial adapter (2)
  - One vial of Humira for injection (3)
  - Two alcohol pads (4)
  - One needle (5)

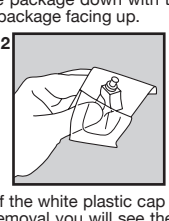
1



- Humira is a clear and colorless liquid. **Do not use** if the liquid is cloudy, discolored or has flakes or particles in it.
- Do not use a frozen vial or a vial that has been left exposed to sunlight.
- Leave the vial on the surface a few minutes before use (15-20 minutes), as it is advisable that Humira reaches room temperature before the injection.

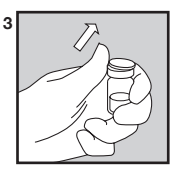
2. Preparing the dose for injection:
Do not discard any of the items until the injection is completed.
- Prepare the needle by partially opening the package. Open the package from the part closest to the yellow end of the needle adapter. Open the package just far enough to expose the yellow part of the needle adapter (see picture number 2).
  Set the package down with the clear side of the package facing up.

2



- Pop off the white plastic cap from the vial. After removal you will see the vial stopper (gray-colored rubber in the center and surrounding silver ring) (see picture number 3).

3



- Use one alcohol pad to wipe the vial stopper (gray rubber). **Do not touch** this vial stopper after wiping it with the alcohol pad.
- Gently peel the entire paper wrapping from the vial adapter package but do not touch and do not remove the vial adapter from the transparent plastic package (see picture number 4). Continue holding it in one hand through the transparent plastic package.

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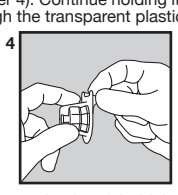

- With your other hand, hold the vial with the stopper facing up.
- With the vial adapter still inside its transparent plastic package, attach its exposed part to the vial stopper by pushing until a click is heard and the whole vial adapter fits over the vial stopper (see left picture below, picture number 5).
- When you are sure that the vial adapter is attached to the vial, lift off the transparent plastic package from the vial adapter (see right picture below, picture number 6).
- Gently return the vial with the vial adapter on it to the clean work surface, taking care that it does not fall. **Do not touch** the vial adapter.

5 6

- Prepare the syringe by partially opening the package. Open the transparent package from the part closest to the white plunger of the syringe until the round part of the white plunger is exposed. Do not remove the syringe from the package.
- Hold the syringe package together with the syringe and **slowly** pull the plunger up to 0.1 ml more than the volume set for administering the dose (for example, if the prescribed dose is 0.5 ml, pull the plunger to 0.6 ml). **Never** pull the plunger past 0.9 ml (see picture number 7).
- Preparation of the dose prescribed for injection by the doctor will be done at a later stage.
- **Do not under any circumstances pull** the white plunger completely out of the syringe.

Note:
If the white plunger is pulled completely out of the syringe, discard the syringe and contact the pharmacist who dispensed the Humira to you or the attending health-care provider (nurse/doctor).
Do not try to reinsert the white plunger into the syringe.

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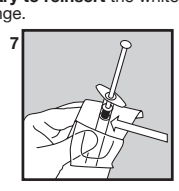

- **Do not hold** the white plunger in order to remove the syringe from the package. Hold the syringe on the graduated area of the body of the syringe and pull the syringe from its package. **Do not press** the plunger down. Continue to hold the syringe in one hand.
- With the other hand, hold the vial adapter firmly at its bottom part, and insert the syringe tip into the upper part of the vial adapter and with a clockwise twisting motion firmly attach the syringe to the adapter. **Do not** over-tighten (see picture number 8).

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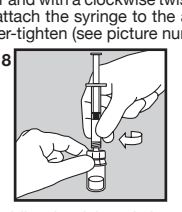

- While holding the vial, push the white plunger all the way down. This is an important step required to prepare the correct dose volume. Hold the white plunger pressed down (see picture number 9) and turn the vial with the syringe upside down (so that the vial is on top and the syringe on the bottom, see picture number 10).

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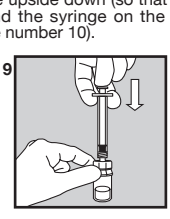
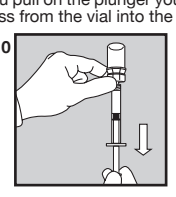


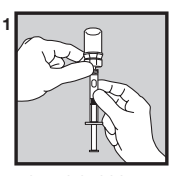
Slowly pull the plunger out to a volume of 0.1 ml beyond the dose prescribed for administration. For example, if the prescribed dose is 0.5 ml, pull the plunger out to 0.6 ml. This is an important step required to prepare the correct dose volume. Withdrawing the dose volume prescribed for injection will be done only in Step 4 - Dose preparation.
When you pull on the plunger you will see the liquid pass from the vial into the syringe.

10



- Push the plunger all the way back in so the liquid will be returned to the vial (see picture number 11).
  Again, **slowly** pull the plunger out to a volume of 0.1 ml beyond the prescribed dose volume for administration.
  This is an important step required to prepare the correct dose volume and to avoid air bubbles or air gaps in the liquid. Preparation of the dose volume prescribed for injection will be done only in Step 4 - Dose preparation.

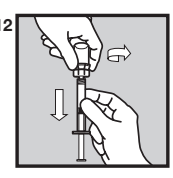
11



- If you see that air bubbles or air gaps have remained in the liquid in the syringe, you should repeat this process of withdrawing and returning of the fluid up to 3 times.
  Do not shake the syringe.

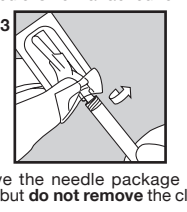
Note:
If the white plunger is pulled completely out of the syringe, discard the syringe and contact the pharmacist who dispensed the Humira to you or the attending health-care provider (nurse/doctor).
Do not try to reinsert the white plunger into the syringe.
- Keep the syringe upright and hold it at the graduated area of its body with one hand. With the other hand, release the vial adapter with the vial from the syringe using a twisting motion.
  Do not touch the tip of the syringe (see picture number 12).

12



- If you see an air bubble or air gap near the syringe tip, **slowly** push the plunger until the fluid in the syringe advances toward the syringe tip. **Do not push** the plunger past the prescribed dose volume.
- For example, if the prescribed dose is 0.5 ml, **do not push** the white plunger past the 0.5 ml position.
- Check to see that the fluid remaining in the syringe is at least the prescribed dose volume. If the volume remaining in the syringe is less than the prescribed dose volume, **do not use** the syringe and contact the pharmacist who dispensed the medicine to you or the attending health-care provider.
- With your free hand, pick up the needle package with the yellow part of the needle adapter facing down.
- Keeping the syringe pointing up, insert the syringe tip into the yellow part of the needle adapter and twist the syringe as indicated by the arrow in the picture (see picture number 13) until the attachment is firm. The needle is now attached to the syringe.

13



- Remove the needle package by pulling gently, but **do not remove** the clear needle cap.
- Place the syringe on the clean work surface. Continue with choosing the injection site and preparation of the prescribed dose volume immediately.

3. Choosing and preparing an injection site:
- Choose an injection site on your thigh or stomach. **Do not choose** the same site that you chose last time (see picture number 14).
- The new injection site should be at least 3 cm away from the last injection site.
- If you choose the stomach - keep a space of 5 cm from the navel.

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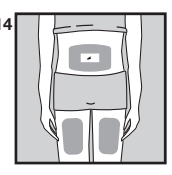

- **Do not inject** in an area where the skin is red, bruised or hard. This may indicate that there is an infection and therefore, you should contact the doctor.
- Some patients find it more comfortable to apply a small ice pack on the area for about two minutes before the injection. In this way the needle insertion is almost not felt. All the preparations and the application of the ice will be done before the injection area is cleaned with alcohol.
- In order to reduce the chance for infection, wipe the injection area with the enclosed alcohol pad.
- **Do not touch** the area again before injecting.

4. Dose preparation:
- With one hand, pick up and hold the syringe with the needle pointing up.
- With the other hand, flip the pink part down toward the syringe (see picture number 15).

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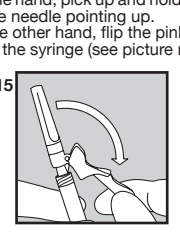

- Carefully remove the clear needle cap by pulling it straight up (see picture number 16).

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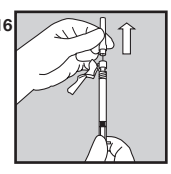

- The needle is clean.
- **Do not touch** the needle.
- **Do not set** the syringe down at any time after the clear needle cap is removed.
- **Do not try** to put the clear needle cap back on the needle.
- Hold the syringe at eye-level with the needle pointing up to see the volume of fluid in the syringe clearly. You must be careful and avoid squirting the liquid towards your eyes.
- Recheck the prescribed dose volume.
- By carefully pushing the plunger into the syringe adjust the volume of liquid to the prescribed dose volume. Excess liquid will come out of the needle while the white plunger is being pushed. **Do not wipe off** the needle or the syringe.

5. Injecting Humira:
- With your free hand, gently grasp the cleaned area of skin and hold it firmly.
- With the other hand, hold the syringe at a 45-degree angle to the skin (see picture number 17).
- With one quick, short motion, push the needle all the way into the skin.
- Let go of the skin in your first hand.
- Be careful not to push the syringe plunger before the needle has been inserted completely.
- Push the plunger to inject the liquid until the syringe is empty.
- When the syringe is empty, remove the needle from the skin, being careful to pull it out at the same angle as when it was inserted.

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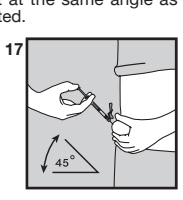
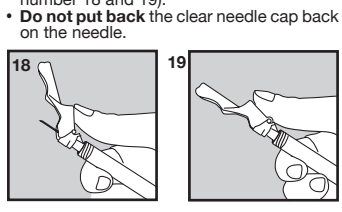


- Gently flip the pink needle cover up over the needle until a click is heard. Place the syringe on the work surface (see pictures number 18 and 19).
- **Do not put back** the clear needle cap back on the needle.

18 19



- Using a piece of gauze, press on the injection site for 10 seconds. There may be light bleeding. **Do not rub** the injection site. Use a plaster if you want to.

6. Waste disposal:
- You will need a special container to collect the syringes after use (ask the doctor/nurse for an appropriate container).
- Throw the syringe with the needle, the vial and vial adapter into the special container for collection of syringes. **Do not throw** these items into the regular household waste.
- **Do not reuse** the Humira syringe, needle, vial and vial adapter.
- Keep this container out of the reach and sight of children.
- Throw away all other used items into your regular household waste.

If you accidentally take too high a dosage
If you accidentally inject a higher dosage of Humira, or if you inject Humira more frequently than told to by the attending doctor or pharmacist, you should call the doctor or pharmacist and inform him about it. For your meeting with the doctor or if you have to go to a hospital emergency room, always take the package of the medicine with you, even if it is empty.

If you accidentally take too low a dosage
If you accidentally inject a lower dose of Humira or if you inject Humira less frequently, you should call the doctor immediately and inform him about it. Always take the package of the medicine with you, even if it is empty.

If you forget to take Humira
If you forget to inject Humira, you should inject the next Humira dose as soon as you remember. Then inject the next dose according to the original schedule, had you not forgotten a dose.

If you stop using Humira
Stopping use of Humira should be discussed with the doctor. The symptoms you suffered from in the past may return upon stopping use of Humira.
Adhere to the treatment as recommended by 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 any further questions regarding the use of the medicine, ask the doctor or pharmacist.

4) SIDE EFFECTS

As with any medicine, use of Humira may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.
Most side effects are mild to moderate. However, some of them may be serious and require treatment. Side effects may occur at least up to 4 months after the last Humira treatment.

Refer to the doctor immediately if you notice one of the following symptoms:
- Severe rash, hives or other signs of allergic reaction.
- Swollen face, hands or feet.
- Difficulty breathing, difficulty swallowing.
- Shortness of breath with exertion or upon lying down or swelling of the feet.

Refer to the doctor as soon as possible if you notice one of the following symptoms:
- Signs indicating an infection, such as: fever, feeling sick, wounds, dental problems, burning upon urination
- Feeling weak or tired
- Cough
- Tingling
- Numbness
- Double vision
- Arm or leg weakness
- A bruise or an open sore that does not heal
- Signs and symptoms indicating blood disorders, such as: persistent fever, bruising, bleeding and paleness

The symptoms described above can be signs of the below listed side effects, which have been observed during treatment with Humira:

Very common side effects (effects that occur in more than 1 in 10 users):
- injection site reactions (including pain, swelling, redness or itching)
- respiratory tract infections (including cold, runny nose, sinus infection, pneumonia)
- headache
- abdominal pain
- nausea and vomiting
- rash
- musculoskeletal pain

Common side effects (effects that occur in 1-10 out of 100 users):
- serious infections (including sepsis and influenza)
- skin infections (including cellulitis and shingles)
- ear infections
- oral infections (including tooth infections and cold sores)
- reproductive tract infections
- urinary tract infections
- fungal infections
- joint infections
- benign tumors
- skin cancer
- allergic reactions (including seasonal allergy)
- dehydration
- mood swings (including depression)
- anxiety
- difficulty sleeping
- sensation disorders, such as: tingling, prickling or numbness
- migraine
- nerve root compression (including low back pain and leg pain)
- vision disturbances
- eye inflammation
- inflammation of the eyelid and eye swelling
- vertigo
- sensation of rapid heartbeat
- high blood pressure
- flushing
- hematoma
- cough
- asthma
- shortness of breath
- gastrointestinal bleeding
- dyspepsia (indigestion, bloating, heart burn)
- acid reflux disease
- sicca syndrome (including dry eyes and dry mouth)
- itching
- itchy rash
- bruising
- inflammation of the skin, such as: eczema
- breaking of fingernails and toenails
- increased sweating
- hair loss
- new onset or worsening of psoriasis
- muscle spasms
- blood in urine
- kidney problems
- chest pain
- edema
- fever
- reduction in blood platelets which increases risk of bleeding and bruising
- impaired healing

Uncommon side effects (effects that occur in 1-10 out of 1,000 users):
- opportunistic infections (including tuberculosis and other infections that occur when resistance to disease is lowered)
- neurological infections (including viral meningitis)
- eye infections
- bacterial infections
- diverticulitis (inflammation and infection of the large intestine)
- cancer
- cancer that affects the lymph system (lymphoma)
- melanoma
- immune system disorders that may affect the lungs, skin and lymph nodes (most commonly presenting as sarcoidosis)
- inflammation of the blood vessels (vasculitis)
- tremor
- neuropathy
- stroke
- double vision
- hearing loss, buzzing
- sensation of irregular heartbeat, such as: skipped beats
- heart problems that may cause shortness of breath or ankle swelling
- heart attack
- a sac in the wall of a major artery, inflammation and clot of a vein, blockage of a blood vessel
- lung diseases causing shortness of breath (including inflammation)
- pulmonary embolism (blockage in an artery of the lung)
- pleural effusion (abnormal collection of fluid in the pleural space)
- inflammation of the pancreas which causes severe pain in the abdomen and back
- difficulty swallowing
- facial edema
- gallbladder inflammation, gallbladder stones
- fatty liver
- night sweats
- scarring
- abnormal muscle breakdown (rhabdomyolysis)
- systemic lupus erythematosus (autoimmune disease that can impair organs of the body, including: inflammation of skin, heart, lung, joints and other organs)
- sleep interruptions
- impotence
- inflammations

Rare side effects (effects that occur in 1-10 out of 10,000 users):
- leukemia (cancer affecting the blood and bone marrow)
- severe allergic reaction with shock
- multiple sclerosis
- nerve disorders, such as: optic nerve inflammation and Guillain-Barré syndrome that may cause muscle weakness, abnormal sensations, tingling in the arms and upper body
- heart stops pumping
- pulmonary fibrosis (scarring of the lung)
- intestinal perforation
- hepatitis
- reactivation of hepatitis B virus
- autoimmune hepatitis (inflammation of the liver caused by the body's own immune system)
- inflammation of blood vessels in the skin
- Stevens-Johnson syndrome (early symptoms include: malaise, fever, headache and rash)
- facial edema associated with allergic reactions
- erythema multiforme (inflammatory skin rash)
- lupus-like syndrome

Side effects of unknown frequency (effects whose frequency has not yet been determined):
- hepatosplenic T-cell lymphoma (a rare blood cancer that often causes death)
- Merkel cell carcinoma (a type of skin cancer)
- liver failure
- worsening of a condition called dermatomyositis (seen as a skin rash accompanying muscle weakness)

Some side effects observed with Humira do not have symptoms and may only be discovered through blood tests. These include:

Very common side effects (effects that occur in more than 1 in 10 users):
- low levels of white blood cells
- low levels of red blood cells
- increased lipids in the blood
- elevated liver enzymes

Common side effects (effects that occur in 1-10 out of 100 users):
- high levels of white blood cells
- low levels of platelets
- increased uric acid in the blood
- abnormal levels of sodium in the blood
- low levels of calcium in the blood
- low levels of phosphate in the blood
- high blood sugar
- high levels of the enzyme lactate dehydrogenase in the blood
- autoantibodies present in the blood

Rare side effects (effects that occur in 1-10 out of 10,000 users):
- low levels of white blood cells, red blood cells and platelets

Side effects of unknown frequency (effects whose frequency has not yet been determined):
- liver failure

If one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult the doctor or pharmacist.

Side effects can be reported to the Ministry of Health by clicking on the link: "Reporting side effects from drug treatment", which can be found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects.

5) HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, and any other medicine, must be kept in a closed place out of the reach and sight of children and/or infants in order to avoid poisoning.
- Do not use the medicine after the expiry date (exp. date) appearing on the outer and inner packages and on the vial. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C-8°C: this temperature range is predominant in most household refrigerators).
- Do not freeze.
- Keep the vial in the outer carton package in order to protect from light.
- Do not throw away medicines via wastewater or household waste. Ask the doctor or pharmacist how to throw away medicines you no longer need. Taking these measures will help protect the environment.

Do not use the medicine if you notice that:
- The name HUMIRA does not appear on the packages.
- Check that the liquid in the vial is clear and colorless. Do not use the vial if the liquid is unclear, is discolored or cloudy.
- Check the expiry date appearing on the outer and inner packages and on the vial. Do not use the medicine after this date.
- Make sure that the package is not damaged and that no items are missing. If the package is damaged or items are missing, do not use Humira and contact the pharmacist in the pharmacy.

6) FURTHER INFORMATION

- In addition to the active ingredient, the medicine also contains:
  Mannitol, sodium chloride, disodium phosphate dihydrate, citric acid monohydrate, polysorbate 80, sodium dihydrogen phosphate dihydrate, sodium citrate, sodium hydroxide and water for injections.
  This medicine contains less than 23 mg sodium per vial, and therefore it is considered 'sodium-free' and does not contain preservatives.
- **What the medicine looks like and the content of the pack?**
- Humira 40 mg is a sterile solution in a volume of 0.8 ml per vial.
- The vial is a glass vial.
- One pack contains 2 boxes, each containing 1 vial, 1 vial adapter, 1 sterile syringe, 1 needle and 2 alcohol pads.
- Humira is available in the following forms: a pre-filled syringe, a pre-filled pen and a single-use vial.
- **License holder and its address:** AbbVie Biopharmaceuticals Ltd., 4 Haharash St., Hod Hasharon, Israel.
- **Manufacturer name and address:** AbbVie Ltd., Maidenhead, England.
- **This leaflet was checked and approved by the Ministry of Health in:** October and November 2015.
- **Registration number of the medicine in the National Drug Registry of the Ministry of Health:** 131-41-30990-00.