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

HADLIMA Solution for Injection

Each Pre-filled swippe/Pre-filled pen contains: Adalimumah 40 mg Inactive ingredients and allergens: See section 6 "Further Information" and in section 2 "Important information reparding some of the ingredients of the medicine"

regarding some on the ingrevening on the instantial Read this leaflet carefully in its entirety before using the medicine.

rarmaost. Is medicine has been prescribed to treat your allment. Do not pass it on to others. It may harm them even if it ems to you that their medical condition is similar.

In addition to the leaflet, there is a "Patient safety information card" for the preparation Hadlima solution for injection. This card contains important safety information, that you should know before starting treatment and during the treatment with Hadlima solution for injection and act accordingly. Refer to the "Patient safety information card" and the patient leaflet before you start using this preparation. The card should be kept for for the accuracy.

For your attention, it is important that each time you receive the medicine at the pharmacy, make sure that you receive the same medicine that your expert doctor prescribed for you. If the medicine you received appears different from the one you normally receive or the instructions of use have charged. please contact the pharmacist immediately to make sure you have received the correct medicine. Any replacement or dosage charge of a medicine containing adalmurate D must be made only by the expert attending doctor. Please check that we horand name of the preparation prescribed by your expert doctor is identical to the made of the week that you received from the pharmacist.

1. WHAT IS THE MEDICINE INTENDED FOR?

Horizon of the intended for the restment of: - moderate to severe, active rheumatoid arthritis in adults, when other accepted treatment has been inadequate. - severe active analysioning spondylits in adults, when other accepted treatment has been inadequate. - severe active analysioning spondylits in adults, when other accepted treatment has been inadequate. - severe active analysioning spondylits in adults, when other accepted treatment has been inadequate. - severe active analysioning spondylits in adults, when other accepted treatment has been inadequate. - active and progressive provide arthritis in adults, when other accepted treatment has been inadequate. - active and progressive provide arthritis in adults, when other accepted treatment has been inadequate. - active, moderate to severe hardnellis supportision in adults, when accepted treatment has been inadequate. - moderate to severe hardnellis supportision in adults, when accepted treatment has been inadequate. - moderate to severe hardnellis supportision in adults, when other accepted treatment has been inadequate.

Inoderate to severe, active Croin's disease in adults, when other accepted treatment has ether been nadequate or is inappropriate.
 active, moderate to severe ulcerative colitis in adults, when other accepted treatment has been inadequate, or in patients who can treceive other accepted treatments.
 uveits – Inflammation of the uvea (panuveits, posterior or Intermediate), from a non-infectious source, in adults, when other accepted treatment with steroids is inappropriate or inadequate.
 Intestinal Behcet's disease in adults, when other accepted treatment has been inadequate.
 Therapeutic group: Immunosuppressant, Tumour Necrosis Factor alpha (TN+a) inhibitor.

Hadlima contains the active substance adalimumab, a medicine that acts on your body's immune (defence)

The target of adalimumab is a protein called tumour necrosis factor (TNFo), which is present at increased levels in the inflammatory diseases listed above. By attaching to TNFo, Hadlima decreases the process of inflammation in theme diseases.

2. BEFORE USING THE MEDICINE

Do not use this medicine ff: • you are sensitive (allergic) to adalimumab or to any of the other ingredients contained in this medicine. For the list of inactive ingredients, see section 6 "Further Information". • you have a servere infection, including ubberculosis (see "Special warnings regarding use of the medicine"). It is important that you tell your doctor if you have symptoms of infections, e.g. fever, wounds, feeling tired, dental problems. • you have moderate or severe heart failure. It is important to tell your doctor if you have had or have a serious heart condition (see "Special warnings regarding use of the medicine").

Special warnings regarding use of the medicine Before taking the medicine, tell your doctor if:

<u>Alleracic reaction</u> If you have **allergic reactions** with symptoms such as chest tightness, whereing, dizviness, swelling or rish, do not insect more it fadima and contact your doctor immediately, since in rare cases, these reactions can be life-threatening.

Infection • If you have an **infection**, including long-term or localised infection (for example, leg ulcer), consult your doctor Involve an infection, including long-term of localised infection for example, leg user), consult your obcross before starting healtimal (you are unsure contactly your doctor.
 You might get infections more easily while you are receiving Hadima treatment. This risk may increase if your lung function is impaired. These infections may be serious and include tuberculosis infections caused by viruse fung), parallels or bargets (health are applied to the serious infections associated with a weakened immune system) and sepsis (blood policinity). In race case, these infections may be life-threatening. It is important to telly our doctor if you get symptoms such as fevel, woundi, feeling tired or dental problems. Your doctor may recommend temporary discontinuous of hadima.

Tuberculosis Tuberculosis have been reported in patients treated with Hadima, your doctor will check you for Sar cases of tuberculosis have been reported in patients treated with Hadima. This will include a thorough med evaluation, including your medical history and screening tests (for example chest X-ray and a tuberculin test). It tests and their results should be documented on your Patient Card. It is very important that you tell your docts you have ever had tuberculosis, or if you have been in close contact with someone who has had tuberculosis. If symptoms of tuberculosis gensiten cough, veght loss, litelssness, mild fever, or any other infection appear during or after therapy, tell your doctor immediately.

<u>Travel/recurrent infections</u> •Tell your doctor if you reside or travel in regions where fungal infections such as histoplasmosis,

coccidioidomycosis or blastomycosis are endemic. • Tell your doctor if you have a history of recurrent infections or other conditions that increase the risk of infections

Hengliks Rylins: Tell your doctor fyou are a carrier of the **Hepatitis B Virus (HBV)**. If you have active HBV Infection or if you think you might be at risk of contracting HBV. Your doctor should test you for HBV. Hadlima can reactivate HBV infection in people who carry this virus. In some cases, especially I you are taking other medicines that suppress the immune system, reactivation of HBV infection can be life-threatening.

Age over 65 years, If you are over 65 years, you may be more susceptible to infections while taking Hadima. You and your doctor should pay special latention for signs of infection while you are being treated with Hadima. It is important to to your doctor if you get symptoms of infections, such as fever, wounds, feeling tifed or dental problems.

Surgery or dental procedure If you are about to have surgery or dental procedures tell your doctor that you are taking Hadlima. Your doctor may recommend temporary discontinuation of Hadlima.

Demelinating disease If you have or develop **demyelinating disease** (a disease that affects the insulating layer around the nerves, such as millighe sciences), your doctor will decide if you should receive or continue to receive Hadima. Tell your doctor immediately if you get symptoms like changes in your vision, weakness in your arms or legs or numbress or tinging) in any part of your body.

Vaccine vaccines contain weekened but live forms of disease-causing bacteria or viruses, and these vaccines Certain vaccines contain weekened but live forms of disease-causing bacteria or viruses, and these vaccines should not be given while receiving Hadima. Check with your doctor before you receive any vaccines. If you receive Hadima while you are pregnant, you baby may be at higher risk for getting an infection for up to about free months after the last cades you cerevised during pregnancy. It is important that you tell you tably solutions and other health care professionals that you used Hadima during your pregnancy so that they can decide when your baby should receive any vaccine.

Har Failure If you have **mid hear failure** and you are being treated with Hadima, you should be closely monitored for your hear failure condition by your doctor. It is important to tell your 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 your feed), you must contact your doctor immediately. Your doctor will decide if you should receive Hadima.

Fever, bruising, bleeding or pallor In some patients the body may fail to produce enough of the blood cells to fight: off infections or help you to stop bleeding. If you develop a fever that does not go away, or you **bruise** or **bleed** very easily or look very **pale**, call your doctor right away. Your doctor may decide to stop treatment.

Span doctor high arways hour doctor may decale to solp treatment. <u>Cancer</u> • There have been very rare cases of certain kinds of **cancer** in children and adults taking Hadlima or other TNF-o blockers. Reopie with more serious herumatoid arhifts who have had the disease for a long time may have a higher than average risk of getting Jymphoma (a cancer that affects the lymph system), and leukaemia (a cancer that affects the blocd and bone marrow). If you take Hadlima the risk of getting Jymphoma leukaemia, or other cancers may increase. In rare cases, a specific and severe type of lymphoma has been observed in patients taking Hadlima. Some of those patients were also treated with the medicines azathloprine or mercaptopurine. Tell your doctor if you are taking azathloprine or mercaptopurine with Hadlima. • In addition, cases of non-medianoma skin cancer have been observed in patients taking Hadlima. Some or addition takes of non-medianoma skin cancer have been observed in patients taking Hadlima. There was of damaged skin appear during or after therapy or if existing marks or areas of damage change appearance, tell wurd doctor.

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On rare occasions, treatment with Hadlima could result in lupus-like syndrome. Contact your doctor if symptoms such as persistent unexplained rash, fever, joint pain or tiredness occur.

Smoking If you are a heavy smoker, you should discuss with your doctor whether treatment with a TNF-a blocker is arrannalism for you (see above in section "Special warnings regarding use of the medicine"). Appropriate on you use 1.1. Children and adolescents Hardlima is not indicated for use in children and adolescents under 18 years of age.

Method and route of administration Hadlima is given by injection under the skin (subcutaneous injection). For instructions for use, refer to section 7

If you accidentally took a higher dosage If you accidentally inject Hadima more frequently than you should, call your doctor or pharmacist and explai that you have texina higher dosage Always take the outer carton of the medicine with you, even if it is emp If a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital bring the package of the

If you forget to take the medicine at the required time

nject yourself, you should inject the next dose of Hadlima as soon as you remember. Then, take as you would have taken it on your originally scheduled day, had you not forgotten a dose. If you stop using Hadlima The decision to stop using Hadlima should be discussed with your doctor. Your symptoms may return upon

stopping treatment. Adhere to the treatment as recommended by the doctor. C = address is on treatment and in which, do not stop treatment with the medicine without consulting the

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take medicine. Wear glasses if you need them. glasses if you need them. If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Hadlima may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them. Most side effects are mild to moderate. However, some may be serious and require treatment. Side effects may occur up to 4 months or more after the last injection of Hadlima. Stop taking the medicine and seek medical advice immediately, if you notice the following side effects: -severe rash, hives or other signs of allergic reaction;

severe rash, hives or other signs of amergic reaction, swollen face, hands, feet, trouble breathing, swallowing; shortness of breath with exertion or upon lying down or swelling of the feet. Tell your doctor as soon as possible if you notice any of the following side effects signs of infection such as fever, feeling sick, wounds, dental problems, burning on u feeling weak or tired.

coughing;
 tingling;

- functions, - double vision arm or leg: - a bump or open sore that doesn't heal; - signs and symptoms suggestive of blood disorders such as persistent fever, bruising, bleeding, pallor, - signs and symptoms suggestive of blood disorders and head where which have been observed. The symptoms described above can be signs of the below listed side effects, which have be adalimumab:

Very common side effects (may affect more than 1 in 10 people): - injection site reactions (including pain, swelling, redness or itching - respiratory tract infections (including cold, runny nose, sinus infect - bandenberg headache; abdominal (belly) pain; nausea and vomiting

in in the muscles.

Common side effects (may affect up to 1 in 10 people): • serious infections (including blood poisoning and influenza); • intestinal infections (including gastroenteritis); • skin infections (including cellulitis and shingles); • avairifiertions: and infections; -mouth infections; (including tooth infections and cold sores); -eproductive tract infections; -urinary tract infections; - joint infections; - joint infections; - joint infections;

benign tumours;

skin cancer;
 allergic reactions (including seasonal allergy);
 dehydration;
 mood swings (including depression);

anxiety; difficulty sleeping; sensation disorders such as tingling, prickling or numbness;

graine; nptoms of nerve root compression (including low back pain and leg pain); on disturbances; e inflammation; lammation of the eyelid and eye swelling;

erigo (sensation of the room spinning); ensation that the heart is beating rapidly; igh blood pressure; ushing; aematoma (a solid swelling with clotted blood);

- asthma; -shortness of breath; -gastrointestinal bleeding; -dyspepsia (indigestion, bloating, heart burn); -acid reflux disease; -sicca syndrome (including dry eyes and dry mouth); -thching:

ching; chy rash;

bruising: inflammation of the skin (such as ecz breaking of finger nails and toe nails; increased sweating; hair loss;

uscle spa

rest pairs, edema (a build up of fluid in the body which causes the affected tissue to swell), duction in blood platelets which increases risk of bleeding or bruising;

Uncommon side effects (may affect up to 1 in 100 people): • opportunistic infections (which include tuberculosis and other infections that occur

opportunistic intections (come is lowered); neurological infections (including viral meningitis); in the entropy: ye intections; actival infoctions; liverticulits (inflammation and infection of the large intestine); ance; including cancer of the lymph system (lymphoma) and melanoma (a type of skin cancer); mmune disorders that could affect the lungs, skin and lymph nodes (most commonly as a condition called

coldosis); sculitis (inflammation of blood vessels);

uropathy (nerve damage);

stroke: Freeing of irregular heartbeats such as missing beats; Feeling of irregular heartbeats such as missing beats; Feeling of irregular heartbeats such as missing beats; Freeing of irregular heartbeats of breath or ankles welling; myocardial infaction; a sac formation in the wall of a major artery, inflammation and dot in a vein; blockage of a blood vessel; Jung diseases causing shortness of breath (including inflammation); pulmorary embolism (blockage in the artery of the lung); - pulmorary embolism (blockage in the artery of the lung); - inflammation of the pances which causes severe pain in the abdomen and back; - difficulty in swallowing; - difficulty in swallowing; - difficulty in swallowing; - mage the severe pain in the abdomen and back; - difficulty in swallowing;

icial oedema; allbladder inflammation, gallbladder stones; tty liver (build up of fat in liver cells); obt samption

; al al muscle breakdown; c luous erythematosus (including inflammation of skin, heart, lung, joints and other organ systems); sleep interruptions;

Rare side effects (may affect up to 1 in 1,000 people): eleukaemia (cancer affecting the blood and bone mare severe allergic reaction with shock;

severe allergic reaction with shock; multiple selections; nerve disorders (such as inflammation of the optic nerve in the eye, and Guillain-Barré syndrome, a condition that may cause muckle weakness, abnormal sensations, tingling in the arms and upper body; heart stops pumping; unimosing logics (scarring of the lung); imesting logiforation;

hepatitis reactivation of hepatitis B; autoimmune hepatitis (inflammation of the liver caused by the body's own immune system); cutaneous vasculitis (inflammation of blood vessels in the skin); "Sevens-Johnson syndrome (carly symptoms include malaise, fever, headache and rash); "facial oedema associated with allergic reactions; erythemar multiforme (inflammatory skin rash);

Iupus-like synarome;
 angioedema (localized swelling of the skin);
 lichenoid skin reaction (itchy reddish-purple skin rash)

sight of children and/or infants, to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor. Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to he last day of that month.

7. Continue to hold

Hold the pen against your skin until the yellow indicator fills the medicatio • Several seconds later you may hear a 2nd click.

After injecting Hadlima, confirm that the entire medication window is yellow. Throw away the used pen in a special container as instructed by your doctor, nur • Not sure if you received your dose? Contact your doctor, nurse or pharmacist.

m completion & dispose the per

You received your dose if..

 \bigcirc

"Entire" window is yellow No medicine leaked out (a small drop is okay)

the last day or una monormal
 <u>Pre-filled syringe/ Pre-filled pen:</u>
 <u>Pre-filled syringe/ Pre-filled pen:</u>
 <u>Pre-filled syringer (2°C – 8°C)</u>. Do not free:

ore in a refrigerator (2°C = 8°C). Uo not neeze: ep the pre-filled syringe/ pre-filled pen in the outer carton in order to protect from light.

Alternative Storage: A single Hadlima pre-filled syringe/ pre-filled pen may be stored at temperatures up to maximum of 25°C for a period of up to 28 days. The syringe or pen must be protected from light and discarded if not used within the

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6. FURTHER INFORMATION

 In addition to the active ingredient, the medicine also contains:
 Sorbitol, I-histidine hydrochloride monohydrate, Sodium citrate dihydrate, I-histidine, Polysorbate 20, Citric acid 20to to the instance of process teach mondydrate, Water for injection. An end what are the contents of the package? Indelma solution for injection in a pre-filled syringe or in a pre-filled pen is dispensed as a clear to opalescent, slowless to pale brown solution of 0.8 ml. ladima is available in packs containing 2 pre-filled syringes or 2 pre-filled pens. Hadlima is available in packs containing 2 pre-filled syringes **Registration Holder and address:** Samsung Bioepis ILLtd, Abba Hillel Silver St, 14, Ramat-Gan **Manufacturer and address:** Biogen (Denmark) Manufacturing ApS, Hillerød, Denmark • Registration number of the medicine in the National Drug Registry of the Ministry of Health:

7. INSTRUCTIONS FOR USE

Follow this instruction guide carefully, and soon you will develop a routine for injecting confidently. Before you inject, ask your doctor or nurse to show you how to use your pre-filled pen. Your doctor or nurse should make sure you can use your pen correctly. Your single-dose pre-filled pen



HADLIMA

medication medication

There is no button on your pre-filled pen. The needle is hidden below the green base. W n vou push the pre-filled pen firmly onto your skin, the injectio

will start automatical

Caring for your pre-filled pen

Store your pen in the refrigerator, but do not freeze it.
Keep your pen in its carton, and away from light.
Keep the pen out of the sight and reach of children. Here disposal - Use each pen only once. Never reuse a pen. - Throw away your used pen in a special container as instructed by your doctor, nurse or pharmacist.

Place your pre-filled pen and alcohol pads on a clean, dry surface

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cies, or expired, do not use it. y see 1 or more bubbles, and that is okay.

4. Choose an injection site & clean skir

.

5. Pull off the clear needle cap

Wait 15-30 minutes for your pre-filled pen to reach to room te

HADLIMA

√ Not expire

Always make sure your medicine is clear, free of particles, and has not expired. If your medication is not clear, free of particles, or expired, do not use it.

Do not remove the cap just vet!

Do not remove the cap just yet!

3. Inspect medicine & expiration dat

No Particles ✓ Clear? ✓ Colourless:

2. Wait 15-30 minute

cautions If you dropped your pen with the cap ON, it is okay to use the pen. If you dropped your pen with the cap OFF, do not use it. The needle might be dirty or damaged. •Do not use a damaged pen.

perature, which helps reduce your pain during

Injection site care . Choose a fatty area for injection: Fatty areas, like your stornach, are generally the best injection sites. Fatty areas are good for inserting the needle correctly.

Trug interactions If you are taking, have recently taken or if you might take, other medicines, including non-pre medicines and nutritional supplements, tell the doctor or pharmacist. Especially (f you are taking Hadima can be taken together with methotrexate or certain disease-modifying anti-theumatic agent (suffasalazine, hydroxychicorquine, feffunctione) and injectable gold preparations), controsteroids or p medications including non-steroidal anti-inflammatory drugs (NSADa).

Do not take Hadlima with medicines containing the following active substances (for the treatment of rhet arthritis), due to increased risk of serious infection:

abatacept f vou have questions, please ask your doctor.

Pregnancy and breast-feeding

Pregnancy and breast-feeding. You should consider using appropriate contraception to prevent pregnancy and continue its use for at least 5 months after the last injection of Hadima. If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice about taking this medicine. I Hadima should only be used during a pregnancy. If needed. According to a study done in pregnancy, there was no higher risk of birth defects when the mother received addimumab addimumab.

adalimumab. Hadima can be used during breast-feeding. If you received Hadima during your pregnancy, your baby may have a higher risk for getting an infection. It is important that you tell your baby doctors and other health care professionals about your use of Hadim during pregnancy, before the baby receives any vaccine for more information on vaccines see in section "Sp ecial

use of the medicine")

Driving and use of machines Hadima may have a minor influence on your ability to drive, ride a bicycle or use machines. After taking Hadilma there may be a fieling that the room is spinning (vertigo) and vision disturbances.

Important information regarding some of the ingredients of the medicine Hadima contains sodium and sorbitol: This medicinal product contains 20 mg sorbitol in each pre-filled syringe/ pre-filled pen. If you have been tol your doctor that you have an intolerance to certain sugars, contact your doctor before taking this medicinal

Also, this medicinal product contains less than 1 mmol of sodium (23 mg) per 0.8 ml dose, which means it is entially 'sodiu

3. HOW SHOULD YOU USE THE MEDICINE?

Aways use this preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and method of treatment. The dosage and method of treatment will be determined by the doctor only.

Do not exceed the recommended dose.

Side effects of unknown frequency (frequency cannot be estimated from available data): hepatosplenic T-cell wynphoma (a rare blood cancer that is often fatal); Merkel cell carcinoma (a type of skin cancer); kaposis sarcoma, a rare cancer related to inflection with human herpes virus 8. Kaposis sarcoma most commonly Kaposi's sarcoma, a rare cancer related appears as purple lesions on the skin. liver failure; g of a condition called dermatomyositis (inflammation of skin and muscles, seen as a skin rash

companying muscle wea

me side effects observed with adalimumab may not have symptoms and may only be discovered through

Very common side effects (may affect more than 1 in 10 people): • low blood measurements for white blood cells; low blood measurements for red blood cells increased lipids in the blood;

Common side effects (may affect up to 1 in 10 people): - high levels of white blood cells; - low platelets levels in the blood; - increased unic acid in the blood; . s for sodiun low levels of phosphate in the blood; low levels of phosphate in the blood; high blood sugar;
 high levels of lactate dehydrogenase in the blood;
 autoantibadies present in the blood;
 low levels of potassium in the blood.

Uncommon side effects (may affect up to 1 in 100 people): • high levels of bilirubin (blood test for liver function).

Rare side effects (may affect up to 1 in 1,000 people): • low levels of white blood cells, red blood cells and platelets

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

Reporting of side effects

de effects can be reported to the Ministry of Health by dicking on the link "Report Side Effects of Drug estiment" found on the Ministry of Health homepage (<u>www.health.gov/l</u>) that directs you to the online form for porting side effects, or by entering the link: troi/ dispetifier health on vi/l. https://sideeffects.health.gov.il/

5. HOW SHOULD THE MEDICINE BE STORED

Avoid poisoning! This medicine, and all other medicines, must be stored in a safe place out of the reach and



HNDUMA'

Carefully pull off the clear needle cap with a metal center fro It is normal to see a few drops of liquid come out of the nee ect, do not put the needle cap back on. This could nd or damage the needle. You might accidentally stick yourself o

Choose an injection site on your body. Your abdomen (except the area around the navel) or thighs are best. Clean your injection site with an alcohol pad. Do not touch the area again before the injection. • Avoid skin that is sore, buised, scarted, scaly, or has red patches.

6. Place green base, press down, and hold



Place the green base (at a 90 degree angle) on your skin, and push the entire pre-filled pen dow the injection. When you push down, the injection starts. You may hear a 1st click.