Adalimab®

Adalimumab INN

Composition

Adalimab® 40 mg injection: Each pre-filled syringe contains 0.8 ml sterile solution of Adalimumab INN 40 mg.

Pharmacology

Adalimumab is a recombinant human IgG1 monoclonal antibody specific for human tumor necrosis factor (TNF). Adalimumab binds specifically to TNF-alpha and blocks its interaction with the p55 and p75 cell surface TNF receptors. Adalimumab also lyses surface TNF expressing cells in vitro in the presence of complement. TNF is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Elevated levels of TNF are found in the synovial fluid of patients with Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis and play an important role in both the pathologic inflammation and the joint destruction that are hallmarks of these diseases. Increased levels of TNF are also found in psoriasis plaques. In Plaque Psoriasis, treatment with Adalimumab may reduce the epidermal thickness and infiltration of inflammatory cells.

Indications

Adalimumab is a tumor necrosis factor (TNF) blocker indicated for treatment of:

- **Rheumatoid Arthritis (RA):** Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active RA
- **Juvenile Idiopathic Arthritis (JIA):** Reducing signs and symptoms of moderately to severely active polyarticular JIA in patients 2 years of age and older
- **Psoriatic Arthritis (PsA):** Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active PsA
- **Ankylosing Spondylitis (AS):** Reducing signs and symptoms in adult patients with active AS
- **Adult Crohn's Disease (CD):** Reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy. Reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab
- **Pediatric Crohn's Disease:** Reducing signs and symptoms and inducing and maintaining clinical remission in patients 6 years of age and older with moderately to severely active Crohn's disease who have had an inadequate response to corticosteroids or immunomodulators such as azathioprine, 6-mercaptopurine, or methotrexate
- **Ulcerative Colitis (UC):** Inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine (6-MP). The effectiveness of Adalimumab has not been established in patients who have lost response to or were intolerant to TNF blockers
- **Plaque Psoriasis (Ps):** The treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy and when other systemic therapies are medically less appropriate
- **Hidradenitis Suppurativa (HS):** The treatment of moderate to severe hidradenitis suppurativa

Dose and Administration

Administered by subcutaneous injection Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis: 40 mg every other week.

Some patients with RA not receiving methotrexate may benefit from increasing the frequency to 40 mg every week.

Juvenile Idiopathic Arthritis:
10 kg (22 lbs) to <15 kg (33 lbs): 10 mg every other week

15 kg (33 lbs) to < 30 kg (66 lbs): 20 mg every other week

≥ 30 kg (66 lbs): 40 mg every other week

Adult Crohn's Disease and Ulcerative Colitis: Initial dose (Day 1): 160 mg (four 40 mg injections in one day or two 40 mg injections per day for two consecutive days), second dose two weeks later (Day 15): 80 mg, Two weeks later (Day 29): Maintenance dose of 40 mg every other week. For patients with Ulcerative Colitis only: Adalimumab should only be continued in patients who have shown evidence of clinical remission by eight weeks (Day 57) of therapy

Pediatric Crohn's Disease

- **17 kg (37 lbs) to < 40 kg (88 lbs.):** Initial dose (Day 1): 80 mg (two 40 mg injections in one day) , Second dose two weeks later (Day 15): 40 mg , Two weeks later (Day 29): Maintenance dose of 20 mg every other week.
- ≥ **40 kg (88 lbs): Initial dose (Day 1):** 160 mg (four 40 mg injections in one day or two 40 mg injections per day for two consecutive days) , Second dose two weeks later (Day 15): 80 mg (two 40 mg injections in one day) , Two weeks later (Day 29): Maintenance dose of 40 mg every other week.
- **Plaque Psoriasis or Adult Uveitis:** 80 mg initial dose, followed by 40 mg every other week starting one week after initial dose.
- Hidradenitis Suppurativa: Adults: Initial dose (Day 1): 160 mg, second dose two weeks later (Day 15): 80 mg, Third (Day 29) and subsequent doses: 40 mg every week. Adolescents (12 years and older) ≥60 kg (132 lbs.): Initial dose (Day 1): 160 mg, second dose two weeks later (Day 15): 80 mg, third (Day 29) and subsequent doses: 40 mg every week. Adolescents (12 years and older) 30 kg (66 lbs.) to <60 kg (132 lbs.): Initial dose (Day 1): 80 mg, second (Day 8) and subsequent doses: 40 mg every other week.

Contraindications

If any hypersensitivity to Adalimumab or to any component of the formulation. In case of sepsis or risk of sepsis. Treatment with Adalimumab should not be initiated in patients with serious active infections, including chronic or localized infection.

Warning and precautions for use

Serious infections: Do not start Adalimab® during an active infection. If an infection develops, monitor carefully, and stop Adalimab® if infection becomes serious.

Invasive fungal infections: For patients who develop a systemic illness on Adalimab®, consider empiric antifungal therapy for those who reside or travel to regions where mycoses are endemic.

Malignancies: Incidence of malignancies was greater in Adalimab®-treated patients than in controls Anaphylaxis or serious allergic reactions may occur.

Hepatitis B virus reactivation: Monitor HBV carriers during and several months after therapy. If reactivation occurs, stop Adalimab® and begin antiviral therapy.

Demyelinating disease: Exacerbation or new onset, may occur.

Cytopenias, pancytopenia: Advise patients to seek immediate medical attention if symptoms develop, and consider stopping Adalimab®.

Heart failure: Worsening or new onset, may occur.

Lupus-like syndrome: Stop Adalimab® if syndrome develops

Tuberculosis: As cases of tuberculosis have been reported in patients treated with Adalimumab, your doctor will check for signs and symptoms of tuberculosis before starting Adalimumab. This may include a thorough medical history, a chest X-ray and a tuberculin test. The conduct of these tests should be recorded on the Patient Alert Card. It is very important that you tell your doctor if you or the child have ever had tuberculosis, or have been in close contact with someone who has had tuberculosis.

If symptoms of tuberculosis (such as persistent cough, weight loss, listlessness, mild fever), or any other infection appear during or after therapy, tell your doctor immediately.

Blood disorders: Seek medical advice immediately if you or the child has any signs or symptoms such as persistent fever, sore throat, bruising, bleeding or paleness. Such symptoms may point to the existence of potentially life-threatening blood disorders, which may require discontinuation of Adalimumab.

Chickenpox: Consult your doctor if you or the child is exposed to chickenpox when using Adalimumab. Your doctor will determine if preventive treatment for chickenpox is appropriate.

Latex: The needle cover is made from latex (dry natural rubber). Contact your doctor before using Adalimumab if the needle cover will be handled by, or Adalimumab will be given to, someone with a known or possible hypersensitivity (allergy) to latex.

Alcohol abuse: Adalimumab should not be used for the treatment of hepatitis related to alcohol abuse. Please tell your doctor if you or the children in your care have a history of alcohol abuse.

Wegener's granulomatosis: Adalimumab is not recommended for the treatment of Wegener's granulomatosis, a rare inflammatory disease. If you or the children in your care have Wegener's granulomatosis, talk to your doctor.

Anti-diabetic medicines: Tell your doctor if you or the children have diabetes or are taking medicines to treat diabetes. Your doctor may decide if you or the child need less anti-diabetic medicine while taking Adalimumab.

Possible side effects

The most common adverse reaction with Adalimumab was injection site reactions (erythema and/or itching, hemorrhage, pain or swelling). The most common adverse reactions leading to discontinuation of Adalimumab in rheumatoid arthritis were clinical flare reaction, rash and pneumonia. Other adverse reactions of Adalimumab includes- Gastrointestinal disorders: Diverticulitis, large bowel perforations including perforations associated with diverticulitis and appendiceal perforations associated with appendicitis, pancreatitis .

General disorders and administration site conditions: Pyrexia

Hepato-biliary disorders: Liver failure, hepatitis

Immune system disorders: Sarcoidosis

Neoplasms benign, malignant and unspecified (including cysts and polyps): Merkel Cell Carcinoma (neuroendocrine carcinoma of the skin)

Nervous system disorders: Demyelinating disorders (e.g., optic neuritis, Guillain-Barré syndrome), cerebrovascular accident

Respiratory disorders: Interstitial lung disease, including pulmonary fibrosis, pulmonary embolism

Skin reactions: Stevens Johnson Syndrome, cutaneous vasculitis, erythema multiforme, new or worsening psoriasis (all sub-types including pustular and palmoplantar), alopecia

Vascular disorders: Systemic vasculitis, deep vein thrombosis.

Pregnancy and lactation

Pregnancy Category B

Adequate and well controlled studies with Adalimumab have not been conducted in pregnant women. Adalimumab is an IgG1 monoclonal antibody and IgG1 is actively transferred across the placenta during the third trimester of pregnancy.

Lactation

Limited data from published literature indicate that Adalimumab is present in low levels in human milk and is not likely to be absorbed by a breastfed infant. However, no data is available on the absorption of Adalimumab from breast milk in newborn or preterm infants. Caution should be exercised when Adalimumab is administered to a nursing woman.

Pediatric Use

Safety and efficacy of Adalimumab in pediatric patients for uses other than polyarticular juvenile idiopathic arthritis (JIA) and pediatric Crohn's disease have not been established.

Overdose

No Dose limiting toxicity was observed during clinical trials. The highest dose level evaluated has been multiple doses of 10 mg/kg, which is 15 times the recommended dose.

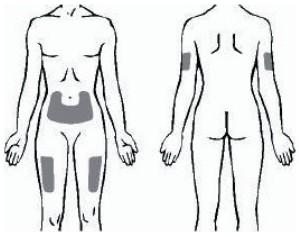
Step 1: Setting up for an injection

1. Select a clean, well-lit, flat working surface.
2. Take the Adalimab® carton containing the pre-filled syringes out of the refrigerator and place it on a flat work surface. Starting from one of the top corners, pull back the paper cover from the top and sides of the tray. Remove pre-filled syringe and one alcohol swab and place them on your work surface. Do not shake the pre-filled syringe of Adalimab®. Please follow last section for instructions on how to store Adalimab®. If you have any questions about storage, contact your doctor, nurse, or pharmacist for further instructions.
3. You should allow 15 to 30 minutes for the Adalimab® solution in the syringe to reach room temperature. Do not remove the needle cover while allowing it to reach room temperature. Waiting until the solution reaches room temperature may make the injection more comfortable for you. Do not warm Adalimab® in any other way (for example, do not warm it in a microwave or in hot water).
4. Assemble the additional supplies you will need for your injection. These include the alcohol swab from the Adalimab® carton and a cotton ball or gauze.
5. Wash your hands with soap and warm water.
6. Inspect the solution in the syringe. It should be clear or slightly opalescent, colourless or pale yellow, and may contain small white or almost transparent particles of protein.This appearance is normal for Adalimab®. Do not use the solution if it is discoloured, cloudy, or if particles other than those described above are present. If you are concerned with the appearance of the solution, then contact your pharmacist for assistance.

Step 2: Choosing an injection site

1. Three recommended injection sites for Adalimab® using a pre-filled syringe include: (1) the front of the middle thighs; (2) the abdomen, except for the 5 cm area right around the navel; and (3) the outer area of the upper arms (see Diagram 1). If you are self injecting, you should not use the outer area of the upper arms.

Diagram 1

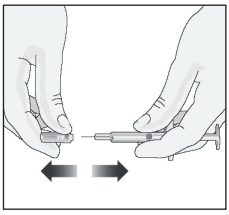


2. A different site should be used for each new injection. Each new injection should be given at least 3 cm from an old site. Do not inject into areas where the skin is tender, bruised, red, or hard. Avoid areas with scars or stretch marks. (It may be helpful to keep notes on the location of the previous injections.)
3. If you have psoriasis, you should try not to inject directly into any raised, thick, red, or scaly skin patches ("psoriasis skin lesions").

Step 3: Injecting the Adalimab® solution

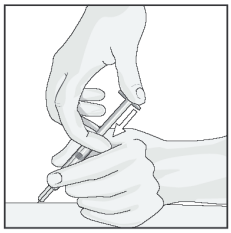
1. Wipe the site where Adalimab® is to be injected with the alcohol swab, using a circular motion. Do not touch this area again before giving the injection.
2. Pick up the pre-filled syringe from the flat work surface. Remove the needle cover by firmly pulling it straight off the syringe (see Diagram 2). Be careful not to bend or twist the cover during removal to avoid damage to the needle. When you remove the needle cover, there may be a drop of liquid at the end of the needle; this is normal. Do not touch the needle or allow it to touch any surface. Do not touch or bump the plunger. Doing so could cause the liquid to leak out.

Diagram 2



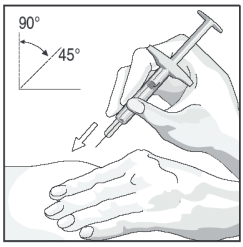
3. When the cleaned area of skin has dried, pinch and hold it firmly with one hand. With the other hand, hold the syringe like a pencil.
4. With a quick, short motion, push the needle all the way into the skin at an angle between 45° and 90° (see Diagram 3). With experience, you will find the angle that is most comfortable for you. Be careful not to push the needle into the skin too slowly, or with great force.

Diagram 3



5. When the needle is completely inserted into the skin, release the skin that you are holding. With your free hand, hold the syringe near its base to stabilise it. Then push the plunger to inject all of the solution at a slow, steady rate (see Diagram 4).

Diagram 4



6. When the syringe is empty, pull the needle out of the skin, being careful to keep it at the same angle as inserted. There may be a little bleeding at the injection site. You can press a cotton ball or gauze over the injection site for 10 seconds. Do not rub the injection site. If needed, you may cover the injection site with a bandage.

Step 4: Disposing of supplies

- The pre-filled syringe is for single-use administration only. The syringe and needle should never be reused. Never recap a needle. Dispose of the needle and syringe as instructed by your doctor, nurse or pharmacist. If you have any questions, please talk to a doctor, nurse or pharmacist who is familiar with Adalimab®.

Commercial pack

Adalimab® 40 mg pre-filled syringe injection: Each box contains 1 pre-filled syringe containing 0.8 ml sterile solution of Adalimumab INN 40 mg and one alcohol pads.

Storage

- Adalimumab should be stored in refrigerator at 2-8 ^{O}C.
- Do not freeze.
- Do not shake.
- Keep away from light.

Medicine: Keep out of reach of children

Healthcare

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