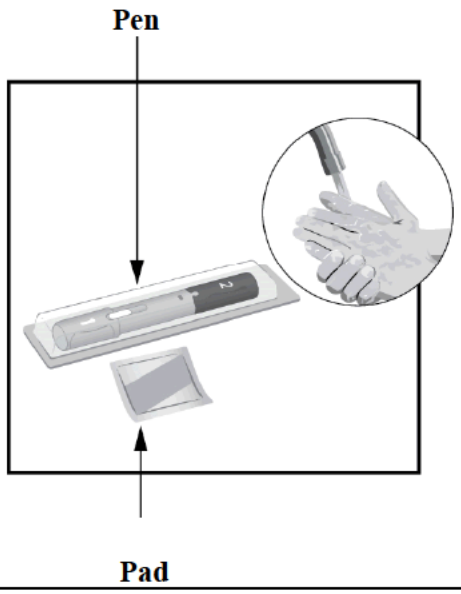
STEP 1

Take Humira out of the refrigerator.

Leave Humira at room temperature for **15 to 30 minutes** before injecting.

- **Do not** remove the Grey or Plum-coloured Caps while allowing Humira to reach room temperature
- **Do not** warm Humira in any other way. For example, **do not** warm it in a microwave or in hot water

STEP 2



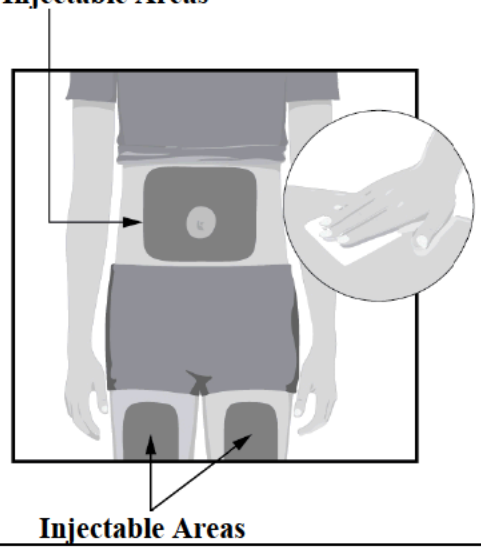
Check expiry (EXP) date. **Do not** use the pre-filled pen if expiry (EXP) date has passed.

Place the following on a clean, flat surface

- 1 single-use pre-filled pen and
- 1 alcohol pad

Wash and dry your hands.

STEP 3



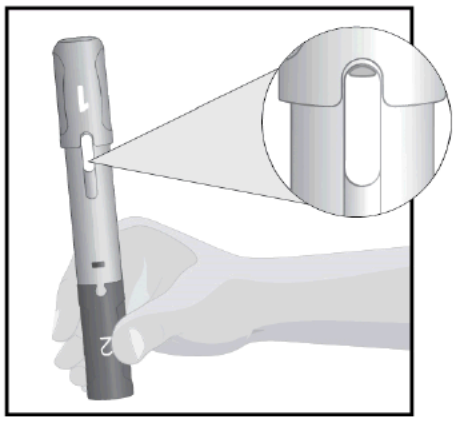
Choose an injection site:

- On the front of your thighs or
- Your belly (abdomen) at least 5 cm from your belly button (navel)
- At least 3 cm from your last injection site

Wipe the injection site in a circular motion with the alcohol pad.

- **Do not** inject through clothes
- **Do not** inject into skin that is sore, bruised, red, hard, scarred, has stretch marks, or areas with psoriasis plaques

STEP 4



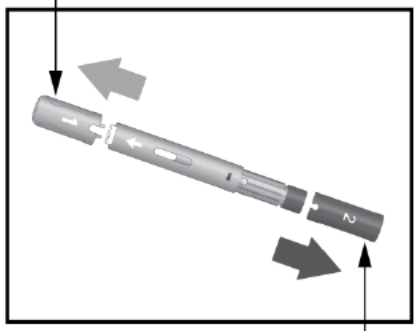
Hold the pre-filled pen with the Grey Cap 1 pointing up.

Check the inspection window.

- It is normal to see 1 or more bubbles in the window
- Make sure the liquid is clear and colourless
- **Do not** use the pre-filled pen if the liquid is cloudy or has particles
- **Do not** use the pre-filled pen if it has been dropped or crushed

STEP 5

Cap 1



Cap 2

Pull the Grey Cap 1 straight off. Throw the cap away. Do not recap.

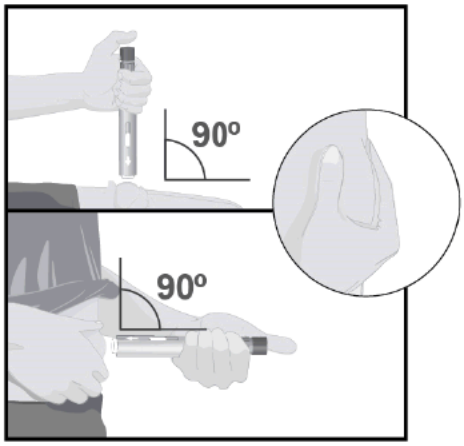
- Check that the small black needle cover of the syringe has been removed with the cap
- It is normal to see a few drops of liquid come out of the needle

Pull the Plum-coloured Cap 2 straight off. Throw the cap away. Do not recap.

The pre-filled pen is now ready to use.

Turn the pre-filled pen so that the white arrow points toward the injection site.

STEP 6



Squeeze the skin at your injection site with your other hand to make a raised area and hold it firmly until the injection is complete.

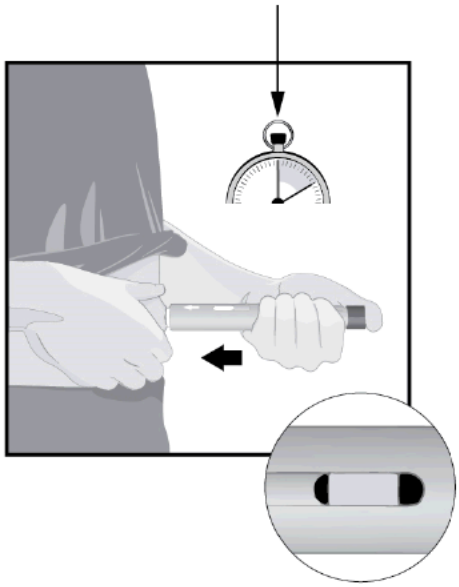
Point the white arrow toward the injection site (thigh or abdomen).

Place the white needle sleeve straight **(90° angle)** against the injection site.

Hold the pre-filled pen so that you can see the inspection window.

Do not press the plum activator button until you are ready to inject.

STEP 7



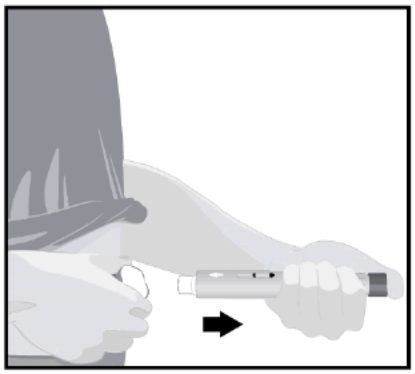
Firmly push the pre-filled pen down against the injection site before starting the injection.
Keep pushing down to prevent the pre-filled pen from moving away from the skin during the injection.

Press the plum activator button and count slowly for **10** seconds.

- A loud **"click"** will signal the start of the injection
- **Keep pushing** the pre-filled pen down **firmly** against the injection site until the injection is complete.

The injection is complete when the yellow indicator has stopped moving.

STEP 8



When the injection is completed, slowly pull the pre-filled pen from the skin. The white needle sleeve will cover the needle tip.

- A small amount of liquid on the injection site is normal

If there are more than a few drops of liquid on the injection site, contact your doctor, nurse or pharmacist.

After completing the injection, place a cotton ball or gauze pad on the skin over the injection site.

- **Do not** rub
- Slight bleeding at the injection site is normal

STEP 9

Throw away the used pre-filled pen in a special disposal container as instructed by your doctor, nurse or pharmacist.

- **Do not** recycle or throw the pre-filled pen in the household waste
- **Always** keep the pre-filled pen and the special disposal container out of the sight and reach of children

The caps, alcohol pad, cotton ball or gauze pad, blister and packaging may be put in your household waste.

Package leaflet: Information for the patient

Humira 80 mg solution for injection in pre-filled syringe
adalimumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- Your doctor will also give you a **Patient Reminder Card**, which contains important safety information that you need to be aware of before you begin using Humira and during treatment with Humira. Keep this **Patient Reminder Card** with you.
- If you have any questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet
1. What Humira is and what it is used for
2. What you need to know before you use Humira
3. How to use Humira
4. Possible side effects
5. How to store Humira
6. Contents of the pack and other information
7. Injecting Humira

1. What Humira is and what it is used for

Humira contains the active substance adalimumab.

Humira is used to treat
- Rheumatoid arthritis
- Plaque psoriasis
- Hidradenitis suppurativa
- Crohn's disease
- Ulcerative colitis
- Non-infectious uveitis

The active ingredient in Humira, adalimumab, is a human monoclonal antibody. Monoclonal antibodies are proteins that attach to a specific target.

The target of adalimumab is a protein called tumour necrosis factor (TNFα), which is involved in the immune (defence) system and is present at increased levels in the inflammatory diseases listed above. By attaching to TNFα, Humira decreases the process of inflammation in these diseases.

Rheumatoid arthritis

Rheumatoid arthritis is an inflammatory disease of the joints.

Humira is used to treat moderate to severe rheumatoid arthritis in adults. You may first be given other disease-modifying medicines, such as methotrexate. If you do not respond well enough to these medicines, you will be given Humira.

Humira can also be used to treat severe, active and progressive rheumatoid arthritis without previous methotrexate treatment.

Humira can slow down the damage to the joints caused by the inflammatory disease and can help them move more freely.

Your doctor will decide if Humira should be used with methotrexate or alone.

Plaque psoriasis

Plaque psoriasis is a skin condition that causes red, flaky, crusty patches of skin covered with silvery scales. Plaque psoriasis can also affect the nails, causing them to crumble, become thickened and lift away from the nail bed which can be painful.

Humira is used to treat moderate to severe chronic plaque psoriasis in adults.

Hidradenitis suppurativa

Hidradenitis suppurativa (sometimes called acne inversa) is a chronic and often painful inflammatory skin disease. Symptoms may include tender nodules (lumps) and abscesses (boils) that may leak pus. It most commonly affects specific areas of the skin, such as under the breasts, the armpits, inner thighs, groin and buttocks. Scarring may also occur in affected areas.

Humira is used to treat
- moderate to severe hidradenitis suppurativa in adults and
- moderate to severe hidradenitis suppurativa in adolescents aged 12to 17 years.

Humira can reduce the number of nodules and abscesses caused by the disease and the pain that is often associated with the disease. You may first be given other medicines. If you do not respond well enough to these medicines, you will be given Humira.

Crohn's disease

Crohn's disease is an inflammatory disease of the digestive tract.

Humira is used to treat
- moderate to severe Crohn's disease in adults and
- moderate to severe Crohn's disease in children and adolescents aged 6 to 17 years.

You may first be given other medicines. If you do not respond well enough to these medicines, you will be given Humira.

Ulcerative colitis

Ulcerative colitis is an inflammatory disease of the large intestine.

Humira is used to treat
- moderate to severe ulcerative colitis in adults and
- moderate to severe ulcerative colitis in children and adolescents aged 6 to 17 years.

You may first be given other medicines. If you do not respond well enough to these medicines, you will be given Humira.

Non-infectious uveitis

Non-infectious uveitis is an inflammatory disease affecting certain parts of the eye.

Humira is used to treat
- adults with non-infectious uveitis with inflammation affecting the back of the eye
- children with chronic non-infectious uveitis from 2 years of age with inflammation affecting the front of the eye

This inflammation may lead to a decrease of vision and/or the presence of floaters in the eye (black dots or wispy lines that move across the field of vision). Humira works by reducing this inflammation. You may first be given other medicines. If you do not respond well enough to these medicines, you will be given Humira.

2. What you need to know before you use Humira

Do not use Humira:

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

- If you have active tuberculosis or other severe infections (see "Warnings and precautions"). It is important that you tell your doctor if you have symptoms of infections, for example, fever, wounds, feeling tired, dental problems.

- If 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 "Warnings and precautions").

Warnings and precautions

Talk to your doctor or pharmacist before using Humira.

Allergic reactions

- If you get allergic reactions with symptoms such as chest tightness, wheezing, dizziness, swelling or rash do not inject more Humira and contact your doctor immediately since, in rare cases, these reactions can be life threatening.

Infections

- If you have an infection, including long-term infection or an infection in one part of the body (for example, leg ulcer) consult your doctor before starting Humira. If you are unsure, contact your doctor.

- You might get infections more easily while you are receiving Humira treatment. This risk may increase if you have problems with your lungs. These infections may be serious and include:
    - tuberculosis

- infections caused by viruses, fungi, parasites or bacteria
- severe infection in the blood (sepsis)

In rare cases, these infections can be life-threatening. It is important to tell your doctor if you get symptoms such as fever, wounds, feeling tired or dental problems. Your doctor may tell you to stop using Humira for some time.

- Tell your doctor if you live or travel in regions where fungal infections (for example, histoplasmosis, coccidioidomycosis or blastomycosis) are very common.

- Tell your doctor if you have had infections which keep coming back or other conditions that increase the risk of infections.

- If you are over 65 years you may be more likely to get infections while taking Humira. You and your doctor should pay special attention to signs of infection while you are being treated with Humira. It is important to tell your doctor if you get symptoms of infections, such as fever, wounds, feeling tired or dental problems.

Tuberculosis

- It is very important that you tell your doctor if you have ever had tuberculosis, or if you have been in close contact with someone who has had tuberculosis. If you have active tuberculosis, do not use Humira.

  - As cases of tuberculosis have been reported in patients treated with Humira, your doctor will check you for signs and symptoms of tuberculosis before starting 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). The conduct and results of these tests should be recorded on your **Patient Reminder Card**.
  - Tuberculosis can develop during therapy even if you have received treatment for the prevention of tuberculosis.
  - If symptoms of tuberculosis (for example, cough that does not go away, weight loss, lack of energy, mild fever), or any other infection appear during or after therapy tell your doctor immediately.

Hepatitis B

- Tell your doctor if you are a carrier of the hepatitis B virus (HBV), if you have active HBV or if you think you might be at risk of getting HBV.

  - Your doctor should test you for HBV. In people who carry HBV, Humira can cause the virus to become active again.
  - In some rare cases, especially if you are taking other medicines that suppress the immune system, reactivation of HBV can be life-threatening.

Surgery or dental procedure

- If you are about to have surgery or dental procedures, please inform your doctor that you are taking Humira. Your doctor may recommend temporary discontinuation of Humira.

Demyelinating disease

This Information is Confidential

- If you have or develop a demyelinating disease (a disease that affects the insulating layer around the nerves, such as multiple sclerosis), your doctor will decide if you should receive or continue to receive Humira. Tell your doctor immediately if you experience symptoms like changes in your vision, weakness in your arms or legs or numbness or tingling in any part of your body.

Vaccinations

- Certain vaccines may cause infections and should not be given while receiving Humira.
    - Check with your doctor before you receive any vaccines.
    - It is recommended that children, if possible, be given all the scheduled vaccinations for their age before they start treatment with Humira.
    - If you received Humira while you were pregnant, your baby may be at higher risk for getting such an infection for up to approximately five months after the last Humira dose you received during pregnancy. It is important that you tell your baby's doctors and other health care professionals about your Humira use during your pregnancy so they can decide when your baby should receive any vaccine.

Heart failure

- If you have mild heart failure and are being treated with Humira, your heart failure status must be closely monitored 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 feet), you must contact your doctor immediately. Your doctor will decide if you should receive Humira.

Fever, bruising, bleeding or looking pale

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

Cancer

- There have been very rare cases of certain kinds of cancer in children and adult patients taking Humira or other TNF blockers.
    - People with more serious rheumatoid arthritis that have had the disease for a long time may have a higher than average risk of getting lymphoma (a cancer that affects the lymph system) and leukaemia (a cancer that affects the blood and bone marrow).
    - If you take Humira the risk of getting lymphoma, leukaemia, or other cancers may increase. On rare occasions, an uncommon and severe type of lymphoma has been seen in patients taking Humira. Some of those patients were also treated with azathioprine or 6-mercaptopurine.
    - Tell your doctor if you are taking azathioprine or 6-mercaptopurine with Humira.
    - Cases of non-melanoma skin cancer have been observed in patients taking Humira.
    - If new skin lesions appear during or after therapy or if existing lesions change appearance, tell your doctor.

- There have been cases of cancers, other than lymphoma in patients with a specific type of lung disease called Chronic Obstructive Pulmonary Disease (COPD) treated with another TNF blocker.

If you have COPD, or are a heavy smoker, you should discuss with your doctor whether treatment with a TNF blocker is appropriate for you.

Autoimmune disease

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

Children and adolescents

- Vaccinations: if possible, children should be up to date with all vaccinations before using Humira.

Other medicines and Humira

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

You should not take Humira with medicines containing the following active substances due to increased risk of serious infection:
- anakinra
- abatacept.

Humira can be taken together with:
- methotrexate
- certain disease-modifying anti-rheumatic agents (for example, sulfasalazine, hydroxychloroquine, leflunomide and injectable gold preparations)
- steroids or pain medications including non-steroidal anti-inflammatory drugs (NSAIDs).

If you have questions, please ask your doctor.

Pregnancy and breast-feeding

- You should consider the use of adequate contraception to prevent pregnancy and continue its use for at least 5 months after the last Humira treatment.
- 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.
- Humira should only be used during a pregnancy if needed.
- According to a pregnancy study, there was no higher risk of birth defects when the mother had received Humira during pregnancy compared with mothers with the same disease who did not receive Humira.
- Humira can be used during breast-feeding.
- If you receive Humira during your pregnancy, your baby may have a higher risk for getting an infection.
- It is important that you tell your baby's doctors and other health care professionals about your Humira use during your pregnancy before the baby receives any vaccine. For more information on vaccines see the "Warnings and precautions" section.

Driving and using machines

Humira may have a small effect on your ability to drive, cycle or use machines. Room spinning sensation and vision disturbances may occur after taking Humira.

3. How to use Humira

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

The recommended doses for Humira in each of the approved uses are shown in the following table. Your doctor may prescribe another strength of Humira if you need a different dose.

Rheumatoid arthritis		
Age or body weight	**How much and how often to take?**	**Notes**
Adults	40 mg every other week	In rheumatoid arthritis, methotrexate is continued while using Humira. If your doctor decides that methotrexate is inappropriate, Humira can be given alone. If you have rheumatoid arthritis and you do not receive methotrexate with your Humira therapy, your doctor may decide to give Humira 40 mg every week or 80 mg every other week.

Plaque psoriasis		
Age or body weight	**How much and how often to take?**	**Notes**
Adults	First dose of 80 mg (one 80 mg injection), followed by 40 mg every other week starting one week after the first dose.	If you have an inadequate response, your doctor may increase the dosage to 40 mg every week or 80 mg every other week.

Hidradenitis suppurativa		
Age or body weight	**How much and how often to take?**	**Notes**
Adults	First dose of 160 mg (two 80 mg injections in one day or one 80 mg injection per day for two consecutive days), followed by an 80 mg dose (one 80 mg injection) two weeks later. After two further weeks, continue with a dose of 40 mg every week or 80 mg every other week, as prescribed by your doctor.	It is recommended that you use an antiseptic wash daily on the affected areas.
Adolescents from 12 to 17 years of age weighing 30 kg or more	First dose of 80 mg (one 80 mg injection), followed by 40 mg every other week starting one week later.	If you have an inadequate response to Humira 40 mg every other week, your doctor may increase the dosage to 40 mg every week or 80 mg every other week. It is recommended that you use an antiseptic wash daily on the affected areas.

Crohn's disease		
Age or body weight	**How much and how often to take?**	**Notes**
Children, adolescents and adults from 6 years of age weighing 40 kg or more	First dose of 80 mg (one 80 mg injection), followed by 40 mg two weeks later. If a faster response is required, the doctor may prescribe a first dose of 160 mg (two 80 mg injections in one day or one 80 mg injection per day for two consecutive days), followed by 80 mg (one 80 mg injection) two weeks later. Thereafter, the usual dose is 40 mg every other week.	Your doctor may increase the dosage to 40 mg every week or 80 mg every other week.

This Information is Confidential

Children and adolescents from 6 to 17 years of age weighing less than 40 kg	First dose of 40 mg, followed by 20 mg two weeks later. If a faster response is required, the doctor may prescribe a first dose of 80 mg (one 80 mg injection), followed by 40 mg two weeks later. Thereafter, the usual dose is 20 mg every other week.	Your doctor may increase the dose frequency to 20 mg every week.

Ulcerative colitis		
Age or body weight	**How much and how often to take?**	**Notes**
Adults	First dose of 160 mg (two 80 mg injections in one day or one 80 mg injection per day for two consecutive days), followed by 80 mg (one 80 mg injection) two weeks later. Thereafter, the usual dose is 40 mg every other week.	Your doctor may increase the dosage to 40 mg every week or 80 mg every other week.
Children and adolescents from 6 years of age weighing less than 40 kg	First dose of 80 mg (one 80 mg injection), followed by 40 mg (one 40 mg injection) two weeks later. Thereafter, the usual dose is 40 mg every other week.	You should continue taking Humira at your usual dose, even after turning 18 years of age.
Children and adolescents from 6 years of age weighing 40 kg or more	First dose of 160 mg (two 80 mg injections in one day or one 80 mg injection per day for two consecutive days), followed by 80 mg (one 80 mg injection) two weeks later. Thereafter, the usual dose is 80 mg every other week.	You should continue taking Humira at your usual dose, even after turning 18 years of age.

Non-infectious uveitis		
Age or body weight	**How much and how often to take?**	**Notes**
Adults	First dose of 80 mg (one 80 mg injection), followed by 40 mg every other week starting one week after the first dose.	Corticosteroids or other medicines that influence the immune system may be continued while using Humira. Humira can also be given alone.
Children and adolescents from 2 years of age weighing less than 30 kg	20 mg every other week	Your doctor may prescribe an initial dose of 40 mg to be administered one week prior to the start of the usual dose of

		20 mg every other week. Humira is recommended for use in combination with methotrexate.
Children and adolescents from 2 years of age weighing 30 kg or more	40 mg every other week	Your doctor may prescribe an initial dose of 80 mg to be administered one week prior to the start of the usual dose of 40 mg every other week. Humira is recommended for use in combination with methotrexate.

Method and route of administration

Humira is administered by injection under the skin (by subcutaneous injection).

Detailed instructions on how to inject Humira are provided in section 7 'Injecting Humira'.

If you use more Humira than you should

If you accidentally inject Humira more frequently than told to by your doctor or pharmacist, call your doctor or pharmacist and tell them that you have taken more. Always take the outer carton of the medicine with you, even if it is empty.

If you forget to use Humira

If you forget to give yourself an injection, you should inject the next dose of Humira as soon as you remember. Then take your next dose as you would have on your originally scheduled day, had you not forgotten a dose.

If you stop using Humira

The decision to stop using Humira should be discussed with your doctor. Your symptoms may return if you stop using Humira.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Most side effects are mild to moderate. However, some may be serious and require treatment. Side effects may occur at least up to 4 months after the last Humira injection.

Tell your doctor immediately if you notice any of the following

- severe rash, hives or other signs of allergic reaction
- swollen face, hands, feet
- trouble breathing, swallowing
- shortness of breath with physical activity or upon lying down or swelling of the feet

This Information is Confidential

Tell your doctor as soon as possible if you notice any of the following

- signs of infection such as fever, feeling sick, wounds, dental problems, burning on urination
- feeling weak or tired
- coughing
- tingling
- numbness
- double vision
- arm or leg weakness
- a bump or open sore that doesn't heal
- signs and symptoms suggestive of blood disorders such as persistent fever, bruising, bleeding, paleness

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

Very common (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 infection, pneumonia)
- headache
- abdominal pain
- nausea and vomiting
- rash
- musculoskeletal pain

Common (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)
- ear infections
- oral infections (including tooth infections and cold sores)
- reproductive tract infections
- urinary tract infection
- fungal 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
- migraine
- nerve root compression (including low back pain and leg pain)
- vision disturbances
- eye inflammation
- inflammation of the eye lid and eye swelling
- vertigo (feeling of dizziness or spinning)

- sensation of heart beating rapidly
- high blood pressure
- flushing
- haematoma (collection of blood outside of blood vessels)
- 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 finger nails and toe nails
- increased sweating
- hair loss
- new onset or worsening of psoriasis
- muscle spasms
- blood in urine
- kidney problems
- chest pain
- oedema (swelling)
- fever
- reduction in blood platelets which increases risk of bleeding or bruising
- impaired healing

Uncommon (may affect up to 1 in 100 people)

- opportunistic infections (which include 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
- melanoma
- immune disorders that could affect the lungs, skin and lymph nodes (most commonly presenting as sarcoidosis)
- vasculitis (inflammation of blood vessels)
- tremor (shaking)
- neuropathy (disorder of the nerves)
- stroke
- hearing loss, buzzing
- sensation of heart beating irregularly such as skipped beats
- heart problems that can 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 in swallowing
- facial oedema (swelling of the face)
- gallbladder inflammation, gallbladder stones
- fatty liver
- night sweats
- scar
- abnormal muscle breakdown
- systemic lupus erythematosus (including inflammation of skin, heart, lung, joints and other organ systems)
- sleep interruptions
- impotence
- inflammations

Rare (may affect up to 1 in 1,000 people)

- leukaemia (cancer affecting the blood and bone marrow)
- severe allergic reaction with shock
- multiple sclerosis
- nerve disorders (such as eye 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 (hole in the intestine)
- 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)
- Stevens-Johnson syndrome (early symptoms include malaise, fever, headache and rash)
- facial oedema (swelling of the face) associated with allergic reactions
- erythema multiforme (inflammatory skin rash)
- lupus-like syndrome
- angioedema (localized swelling of the skin)
- lichenoid skin reaction (itchy reddish-purple skin rash)

Not known (frequency cannot be estimated from the available data)

- hepatosplenic T-cell lymphoma (a rare blood cancer that is often fatal)
- Merkel cell carcinoma (a type of skin cancer)
- Kaposi's sarcoma, a rare cancer related to infection with human herpes virus 8. Kaposi's sarcoma most commonly appears as purple lesions on the skin
- liver failure
- worsening of a condition called dermatomyositis (seen as a skin rash accompanying muscle weakness)
- weight gain (for most patients, the weight gain was small)

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

Very common (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
- elevated liver enzymes

Common (may affect up to 1 in 10 people)

- high blood measurements for white blood cells
- low blood measurements for platelets
- increased uric acid in the blood
- abnormal blood measurements for sodium
- low blood measurements for calcium
- low blood measurements for phosphate
- high blood sugar
- high blood measurements for lactate dehydrogenase
- autoantibodies present in the blood
- low blood potassium

Uncommon (may affect up to 1 in 100 people)

- elevated bilirubin measurement (liver blood test)

Rare (may affect up to 1 in 1,000 people)

- low blood measurements for white blood cells, red blood cells and platelet count

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Humira

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

Do not use this medicine after the expiry date stated on the label/blister/carton after EXP.

Store in a refrigerator (2°C – 8°C). Do not freeze.

Keep the pre-filled syringe in the outer carton in order to protect from light.

Alternative Storage:

When needed (for example when you are travelling), a single Humira pre-filled syringe may be stored at room temperature (up to 25°C) for a maximum period of 14 days – be sure to protect it from light. Once removed from the refrigerator for room temperature storage, the syringe **must be used within 14 days or discarded**, even if it is returned to the refrigerator.

This Information is Confidential

You should record the date when the syringe is first removed from refrigerator and the date after which it should be discarded.

Do not throw away any medicines via wastewater or household waste. Ask your doctor or pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Humira contains

The active substance is adalimumab.
The other ingredients are mannitol, polysorbate 80 and water for injections.

What the Humira pre-filled syringe looks like and contents of the pack

Humira 80 mg solution for injection in pre-filled syringe is supplied as a sterile solution of 80 mg adalimumab dissolved in 0.8 ml solution.

The Humira pre-filled syringe is a glass syringe containing a solution of adalimumab.

The Humira pre-filled syringe is available in a pack containing 1 pre-filled syringe for patient use with 1 alcohol pad.

Humira may be available as a vial, a pre-filled syringe and/or a pre-filled pen.

Marketing Authorisation Holder

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

Manufacturer

AbbVie Biotechnology GmbH
Knollstrasse
67061 Ludwigshafen
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
AbbVie SA
Tél/Tel: +32 10 477811

България
АбВи ЕООД
Тел.:+359 2 90 30 430

Česká republika
AbbVie s.r.o.
Tel: +420 233 098 111

Lietuva
AbbVie UAB
Tel: +370 5 205 3023

Luxembourg/Luxemburg
AbbVie SA
Belgique/Belgien
Tél/Tel: +32 10 477811

Magyarország
AbbVie Kft.
Tel.:+36 1 455 8600

Danmark
AbbVie A/S
Tlf: +45 72 30-20-28
Deutschland
AbbVie Deutschland GmbH & Co. KG
Tel: 00800 222843 33 (gebührenfrei)
Tel: +49 (0) 611 / 1720-0
Eesti
AbbVie OÜ
Tel: +372 623 1011
Ελλάδα
AbbVie ΦΑΡΜΑΚΕΥΤΙΚΗ Α.Ε.
Τηλ: +30 214 4165 555
España
AbbVie Spain, S.L.U.
Tel: +34 91 384 09 10
France
AbbVie
Tél: +33 (0) 1 45 60 13 00

Hrvatska
AbbVie d.o.o.
Tel + 385 (0)1 5625 501
Ireland
AbbVie Limited
Tel: +353 (0)1 4287900
Ísland
Vistor hf.
Tel: +354 535 7000
Italia
AbbVie S.r.l.
Tel: +39 06 928921
Κύπρος
Lifepharma (Z.A.M.) Ltd
Τηλ.: +357 22 34 74 40
Latvija
AbbVie SIA
Tel: +371 67605000

Malta
V.J.Salomone Pharma Limited
Tel: +356 22983201
Nederland
AbbVie B.V.
Tel: +31 (0)88 322 2843

Norge
AbbVie AS
Tlf: +47 67 81 80 00
Österreich
AbbVie GmbH
Tel: +43 1 20589-0
Polska
AbbVie Polska Sp. z o.o.
Tel.: +48 22 372 78 00
Portugal
AbbVie, Lda.
Tel: +351 (0)21 1908400

România
AbbVie S.R.L.
Tel: +40 21 529 30 35
Slovenija
AbbVie Biofarmacevtska družba d.o.o.
Tel: +386 (1)32 08 060
Slovenská republika
AbbVie s.r.o.
Tel: +421 2 5050 0777
Suomi/Finland
AbbVie Oy
Puh/Tel: +358 (0)10 2411 200
Sverige
AbbVie AB
Tel: +46 (0)8 684 44 600
United Kingdom (Northern Ireland)
AbbVie Deutschland GmbH & Co. KG
Tel: +44 (0)1628 561090

This leaflet was last revised in

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

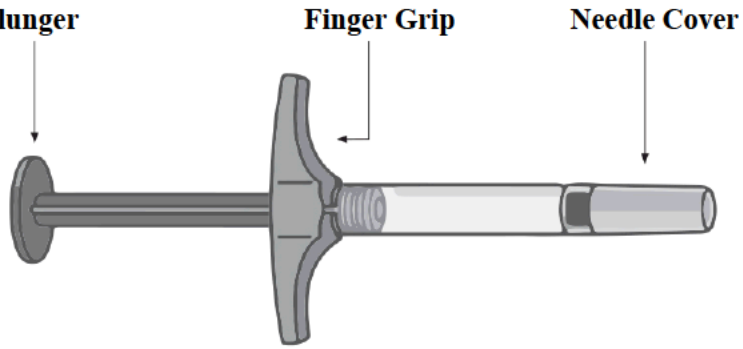
To listen to or request a copy of this leaflet in <Braille>, <large print> or <audio>, please contact the local representative of the Marketing Authorisation Holder.

7. Injecting Humira

- The following instructions explain how to give yourself a subcutaneous injection of Humira using the pre-filled syringe. First read all the instructions carefully and then follow them step by step.

- You will be instructed by your doctor, nurse or pharmacist on the technique of self-injection.
- Do not attempt to self-inject until you are sure that you understand how to prepare and give the injection.
- After proper training, the injection can be given by yourself or given by another person, for example, a family member or friend.
- Only use each pre-filled syringe for one injection.

Humira Pre-filled Syringe



Do not use the pre-filled syringe and call your doctor or pharmacist if the

- liquid is cloudy, discoloured, or has flakes or particles in it
- expiry (EXP) date has passed
- liquid has been frozen or left in direct sunlight
- pre-filled syringe has been dropped or crushed

Do not remove the needle cover until just before injection. Keep Humira out of the sight and reach of children.

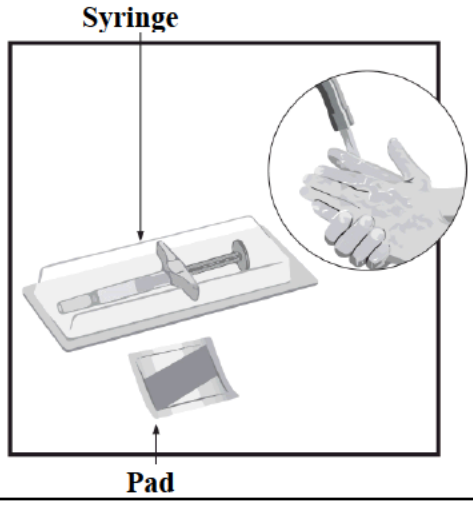
STEP 1

Take Humira out of the refrigerator.

Leave Humira at room temperature for **15 to 30 minutes** before injecting.

- **Do not** remove the needle cover while allowing Humira to reach room temperature
- **Do not** warm Humira in any other way. For example, **do not** warm it in a microwave or in hot water

STEP 2



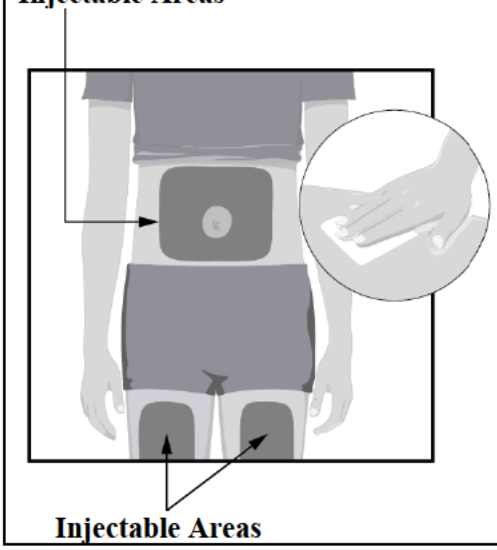
Check the expiry (EXP) date. **Do not** use the pre-filled syringe if expiry (EXP) date has passed.

Place the following on a clean, flat surface

- 1 single-use pre-filled syringe and
- 1 alcohol pad

Wash and dry your hands.

STEP 3



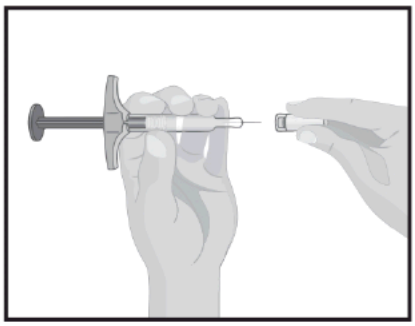
Choose an injection site:

- On the front of your thighs or
- Your belly (abdomen) at least 5 cm from your belly button (navel)
- At least 3 cm from your last injection site

Wipe the injection site in a circular motion with the alcohol pad.

- **Do not** inject through clothes
- **Do not** inject into skin that is sore, bruised, red, hard, scarred, has stretch marks, or areas with psoriasis plaques

STEP 4



Hold the pre-filled syringe in one hand.

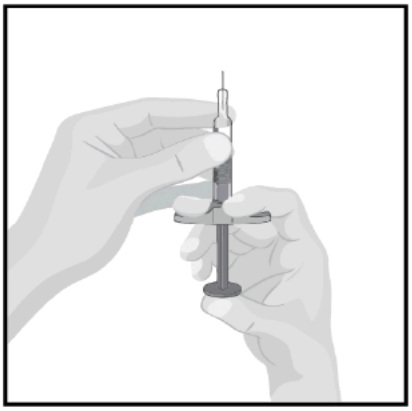
Check the liquid in the pre-filled syringe.

- Make sure the liquid is clear and colourless
- **Do not** use the pre-filled syringe if the liquid is cloudy or has particles
- **Do not** use the pre-filled syringe if it has been dropped or crushed

Gently pull the needle cover straight off with the other hand. Throw the needle cover away. Do not recap.

- **Do not** touch the needle with your fingers or let the needle touch anything

STEP 5



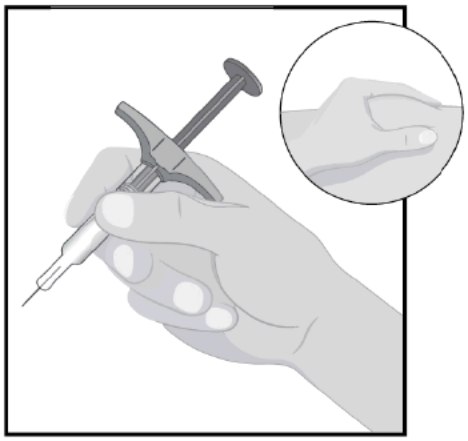
Hold the pre-filled syringe with the needle facing up.

- Hold the pre-filled syringe at eye level with one hand so you can see the air in the pre-filled syringe

Slowly push the plunger in to push the air out through the needle.

- It is normal to see a drop of liquid at the end of the needle

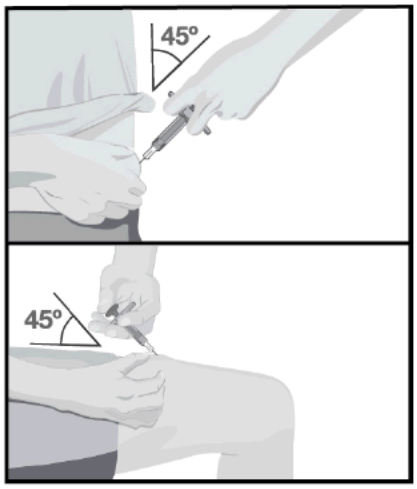
STEP 6



Hold the body of the pre-filled syringe in one hand between the thumb and index fingers, like you would a pencil.

Squeeze the skin at your injection site with your other hand to make a raised area and hold it firmly.

STEP 7

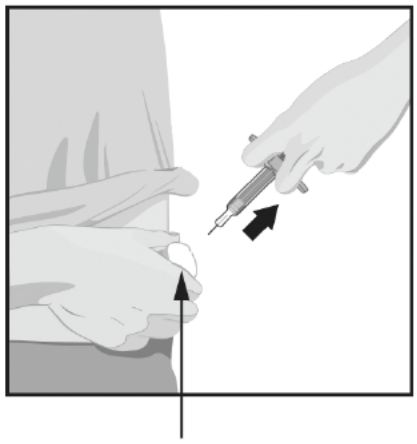


Insert the needle all the way into the skin at about a 45-degree angle with one quick, short motion.

- After the needle is in, let go of the skin you are holding

Slowly push the plunger all the way in until all of the liquid is injected and the pre-filled syringe is empty.

STEP 8



Cotton Ball

When the injection is completed, slowly pull the needle out of the skin while keeping the pre-filled syringe at the same angle.

After completing the injection, place a cotton ball or gauze pad on the skin over the injection site.

- **Do not** rub
- Slight bleeding at the injection site is normal

STEP 9

Throw away the used pre-filled syringe in a special disposal container as instructed by your doctor, nurse or pharmacist. **Never** recap a needle.

- **Do not** recycle or throw the pre-filled syringe in the household waste
- **Always** keep the pre-filled syringe and the special disposal container out of the sight and reach of children

The needle cover, alcohol pad, cotton ball or gauze pad, blister and packaging may be put in your household waste.

Package leaflet: Information for the patient

Humira 80 mg solution for injection in pre-filled pen
adalimumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- Your doctor will also give you a **Patient Reminder Card**, which contains important safety information that you need to be aware of before you begin using Humira and during treatment with Humira. Keep this **Patient Reminder Card** with you.
- If you have any questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet
1. What Humira is and what it is used for
2. What you need to know before you use Humira
3. How to use Humira
4. Possible side effects
5 How to store Humira
6. Contents of the pack and other information
7. Injecting Humira

1. What Humira is and what it is used for

Humira contains the active substance adalimumab.

Humira is used to treat
- Rheumatoid arthritis
- Plaque psoriasis
- Hidradenitis suppurativa
- Crohn's disease
- Ulcerative colitis
- Non-infectious uveitis

The active ingredient in Humira, adalimumab, is a human monoclonal antibody. Monoclonal antibodies are proteins that attach to a specific target.

The target of adalimumab is a protein called tumour necrosis factor (TNFα), which is involved in the immune (defence) system and is present at increased levels in the inflammatory diseases listed above. By attaching to TNFα, Humira decreases the process of inflammation in these diseases.

Rheumatoid arthritis

Rheumatoid arthritis is an inflammatory disease of the joints.

Humira is used to treat moderate to severe rheumatoid arthritis in adults. You may first be given other disease-modifying medicines, such as methotrexate. If you do not respond well enough to these medicines, you will be given Humira.

Humira can also be used to treat severe, active and progressive rheumatoid arthritis without previous methotrexate treatment.

Humira can slow down the damage to the joints caused by the inflammatory disease and can help them move more freely.

Your doctor will decide if Humira should be used with methotrexate or alone.

Plaque psoriasis

Plaque psoriasis is a skin condition that causes red, flaky, crusty patches of skin covered with silvery scales. Plaque psoriasis can also affect the nails, causing them to crumble, become thickened and lift away from the nail bed which can be painful.

Humira is used to treat moderate to severe chronic plaque psoriasis in adults.

Hidradenitis suppurativa

Hidradenitis suppurativa (sometimes called acne inversa) is a chronic and often painful inflammatory skin disease. Symptoms may include tender nodules (lumps) and abscesses (boils) that may leak pus. It most commonly affects specific areas of the skin, such as under the breasts, the armpits, inner thighs, groin and buttocks. Scarring may also occur in affected areas.

Humira is used to treat
- moderate to severe hidradenitis suppurativa in adults and
- moderate to severe hidradenitis suppurativa in adolescents aged 12 to 17 years.

Humira can reduce the number of nodules and abscesses caused by the disease and the pain that is often associated with the disease. You may first be given other medicines. If you do not respond well enough to these medicines, you will be given Humira.

Crohn's disease

Crohn's disease is an inflammatory disease of the digestive tract.

Humira is used to treat
- moderate to severe Crohn's disease in adults and
- moderate to severe Crohn's disease in children and adolescents aged 6 to 17 years.

You may first be given other medicines. If you do not respond well enough to these medicines, you will be given Humira.

Ulcerative colitis

Ulcerative colitis is an inflammatory disease of the large intestine.

Humira is used to treat
- moderate to severe ulcerative colitis in adults and
- moderate to severe ulcerative colitis in children and adolescents aged 6 to 17 years.

This Information is Confidential

You may first be given other medicines. If you do not respond well enough to these medicines, you will be given Humira.

Non-infectious uveitis

Non-infectious uveitis is an inflammatory disease affecting certain parts of the eye.

Humira is used to treat
- adults with non-infectious uveitis with inflammation affecting the back of the eye
- children with chronic non-infectious uveitis from 2 years of age with inflammation affecting the front of the eye

This inflammation may lead to a decrease of vision and/or the presence of floaters in the eye (black dots or wispy lines that move across the field of vision). Humira works by reducing this inflammation. You may first be given other medicines. If you do not respond well enough to these medicines, you will be given Humira.

2. What you need to know before you use Humira

Do not use Humira:

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

- If you have active tuberculosis or other severe infections (see "Warnings and precautions"). It is important that you tell your doctor if you have symptoms of infections, for example, fever, wounds, feeling tired, dental problems.

- If 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 "Warnings and precautions").

Warnings and precautions

Talk to your doctor or pharmacist before using Humira.

Allergic reactions

- If you get allergic reactions with symptoms such as chest tightness, wheezing, dizziness, swelling or rash do not inject more Humira and contact your doctor immediately since, in rare cases, these reactions can be life threatening.

Infections

- If you have an infection, including long-term infection or an infection in one part of the body (for example, leg ulcer) consult your doctor before starting Humira. If you are unsure, contact your doctor.

- You might get infections more easily while you are receiving Humira treatment. This risk may increase if you have problems with your lungs. These infections may be serious and include:
    - tuberculosis

- infections caused by viruses, fungi, parasites or bacteria
- severe infection in the blood (sepsis)

In rare cases, these infections can be life-threatening. It is important to tell your doctor if you get symptoms such as fever, wounds, feeling tired or dental problems. Your doctor may tell you to stop using Humira for some time.

- Tell your doctor if you live or travel in regions where fungal infections (for example, histoplasmosis, coccidioidomycosis or blastomycosis) are very common.

- Tell your doctor if you have had infections which keep coming back or other conditions that increase the risk of infections.

- If you are over 65 years you may be more likely to get infections while taking Humira. You and your doctor should pay special attention to signs of infection while you are being treated with Humira. It is important to tell your doctor if you get symptoms of infections, such as fever, wounds, feeling tired or dental problems.

Tuberculosis

- It is very important that you tell your doctor if you have ever had tuberculosis, or if you have been in close contact with someone who has had tuberculosis. If you have active tuberculosis, do not use Humira.

  - As cases of tuberculosis have been reported in patients treated with Humira, your doctor will check you for signs and symptoms of tuberculosis before starting 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). The conduct and results of these tests should be recorded on your **Patient Reminder Card**.
  - Tuberculosis can develop during therapy even if you have received treatment for the prevention of tuberculosis.
  - If symptoms of tuberculosis (for example, cough that does not go away, weight loss, lack of energy, mild fever), or any other infection appear during or after therapy tell your doctor immediately.

Hepatitis B

- Tell your doctor if you are a carrier of the hepatitis B virus (HBV), if you have active HBV or if you think you might be at risk of getting HBV.
  - Your doctor should test you for HBV. In people who carry HBV, Humira can cause the virus to become active again.
  - In some rare cases, especially if you are taking other medicines that suppress the immune system, reactivation of HBV can be life-threatening.

Surgery or dental procedure

- If you are about to have surgery or dental procedures please inform your doctor that you are taking Humira. Your doctor may recommend temporary discontinuation of Humira.

Demyelinating disease

- If you have or develop a demyelinating disease (a disease that affects the insulating layer around the nerves, such as multiple sclerosis), your doctor will decide if you should receive or continue to receive Humira. Tell your doctor immediately if you experience symptoms like changes in your vision, weakness in your arms or legs or numbness or tingling in any part of your body.

Vaccinations

- Certain vaccines may cause infections and should not be given while receiving Humira.
    - Check with your doctor before you receive any vaccines.
    - It is recommended that children, if possible, be given all the scheduled vaccinations for their age before they start treatment with Humira.
    - If you received Humira while you were pregnant, your baby may be at higher risk for getting such an infection for up to approximately five months after the last Humira dose you received during pregnancy. It is important that you tell your baby's doctors and other health care professionals about your Humira use during your pregnancy so they can decide when your baby should receive any vaccine.

Heart failure

- If you have mild heart failure and are being treated with Humira, your heart failure status must be closely monitored 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 feet), you must contact your doctor immediately. Your doctor will decide if you should receive Humira.

Fever, bruising, bleeding or looking pale

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

Cancer

- There have been very rare cases of certain kinds of cancer in children and adult patients taking Humira or other TNF blockers.
    - People with more serious rheumatoid arthritis that have had the disease for a long time may have a higher than average risk of getting lymphoma (a cancer that affects the lymph system) and leukaemia (a cancer that affects the blood and bone marrow).
    - If you take Humira the risk of getting lymphoma, leukaemia, or other cancers may increase. On rare occasions, an uncommon and severe type of lymphoma, has been seen in patients taking Humira. Some of those patients were also treated with azathioprine or 6-mercaptopurine.
    - Tell your doctor if you are taking azathioprine or 6-mercaptopurine with Humira.
    - Cases of non-melanoma skin cancer have been observed in patients taking Humira.
    - If new skin lesions appear during or after therapy or if existing lesions change appearance, tell your doctor.

- There have been cases of cancers, other than lymphoma in patients with a specific type of lung disease called Chronic Obstructive Pulmonary Disease (COPD) treated with another TNF blocker.

If you have COPD, or are a heavy smoker, you should discuss with your doctor whether treatment with a TNF blocker is appropriate for you.

Autoimmune disease

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

Children and adolescents

- Vaccinations: if possible, children should be up to date with all vaccinations before using Humira.

Other medicines and Humira

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

You should not take Humira with medicines containing the following active substances due to increased risk of serious infection:
- anakinra
- abatacept.

Humira can be taken together with:
- methotrexate
- certain disease-modifying anti-rheumatic agents (for example, sulfasalazine, hydroxychloroquine, leflunomide and injectable gold preparations)
- steroids or pain medications including non-steroidal anti-inflammatory drugs (NSAIDs).

If you have questions, please ask your doctor.

Pregnancy and breast-feeding

- You should consider the use of adequate contraception to prevent pregnancy and continue its use for at least 5 months after the last Humira treatment.
- 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.
- Humira should only be used during a pregnancy if needed.
- According to a pregnancy study, there was no higher risk of birth defects when the mother had received Humira during pregnancy compared with mothers with the same disease who did not receive Humira.
- Humira can be used during breast-feeding.
- If you receive Humira during your pregnancy, your baby may have a higher risk for getting an infection.
- It is important that you tell your baby's doctors and other health care professionals about your Humira use during your pregnancy before the baby receives any vaccine. For more information on vaccines see the "Warnings and precautions" section.

Driving and using machines

Humira may have a small effect on your ability to drive, cycle or use machines. Room spinning sensation and vision disturbances may occur after taking Humira.

3. How to use Humira

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

The recommended doses for Humira in each of the approved uses are shown in the following table. Your doctor may prescribe another strength of Humira if you need a different dose.

Rheumatoid arthritis		
Age or body weight	**How much and how often to take?**	**Notes**
Adults	40 mg every other week	In rheumatoid arthritis, methotrexate is continued while using Humira. If your doctor decides that methotrexate is inappropriate, Humira can be given alone. If you have rheumatoid arthritis and you do not receive methotrexate with your Humira therapy, your doctor may decide to give Humira 40 mg every week or 80 mg every other week.

Plaque psoriasis		
Age or body weight	**How much and how often to take?**	**Notes**
Adults	First dose of 80 mg (one 80 mg injection), followed by 40 mg every other week starting one week after the first dose.	If you have an inadequate response, your doctor may increase the dosage to 40 mg every week or 80 mg every other week.

Hidradenitis suppurativa		
Age or body weight	**How much and how often to take?**	**Notes**
Adults	First dose of 160 mg (two 80 mg injections in one day or one 80 mg injection per day for two consecutive days), followed by an 80 mg dose (one 80 mg injection) two weeks later. After two further weeks, continue with a dose of 40 mg every week or 80 mg every other week, as prescribed by your doctor.	It is recommended that you use an antiseptic wash daily on the affected areas.

Adolescents from 12 to 17 years of age weighing 30 kg or more	First dose of 80 mg (one 80 mg injection), followed by 40 mg every other week starting one week later.	If you have an inadequate response to Humira 40 mg every other week, your doctor may increase the dosage to 40 mg every week or 80 mg every other week. It is recommended that you use an antiseptic wash daily on the affected areas.

Crohn's disease		
Age or body weight	**How much and how often to take?**	**Notes**
Children, adolescents and adults from 6 to 17 years of age weighing 40 kg or more	First dose of 80 mg (one 80 mg injection), followed by 40 mg two weeks later. If a faster response is required, the doctor may prescribe a first dose of 160 mg (two 80 mg injections in one day or one 80 mg injection per day for two consecutive days), followed by 80 mg (one 80 mg injection) two weeks later. Thereafter, the usual dose is 40 mg every other week.	Your doctor may increase the dosage to 40 mg every week or 80 mg every other week.
Children and adolescents from 6 to 17 years of age weighing less than 40 kg	First dose of 40 mg, followed by 20 mg two weeks later. If a faster response is required, the doctor may prescribe a first dose of 80 mg (one 80 mg injection), followed by 40 mg two weeks later. Thereafter, the usual dose is 20 mg every other week.	Your doctor may increase the dose frequency to 20 mg every week.

Ulcerative colitis		
Age or body weight	**How much and how often to take?**	**Notes**
Adults	First dose of 160 mg (two 80 mg injections in one day or one 80 mg injection per day for two consecutive days), followed by 80 mg (one 80 mg injection) two weeks later. Thereafter, the usual dose is 40 mg every other week.	Your doctor may increase the dosage to 40 mg every week or 80 mg every other week.

Children and adolescents from 6 years of age weighing less than 40 kg	First dose of 80 mg (one 80 mg injection), followed by 40 mg (one 40 mg injection) two weeks later. Thereafter, the usual dose is 40 mg every other week.	You should continue taking Humira at your usual dose, even after turning 18 years of age.
Children and adolescents from 6 years of age weighing 40 kg or more	First dose of 160 mg (two 80 mg injections in one day or one 80 mg injection per day for two consecutive days), followed by 80 mg (one 80 mg injection) two weeks later. Thereafter, the usual dose is 80 mg every other week.	You should continue taking Humira at your usual dose, even after turning 18 years of age.

Non-infectious uveitis		
Age or body weight	**How much and how often to take?**	**Notes**
Adults	First dose of 80 mg (one 80 mg injection), followed by 40 mg every other week starting one week after the first dose.	Corticosteroids or other medicines that influence the immune system may be continued while using Humira. Humira can also be given alone.
Children and adolescents from 2 years of age weighing less than 30 kg	20 mg every other week	Your doctor may prescribe an initial dose of 40 mg to be administered one week prior to the start of the usual dose of 20 mg every other week. Humira is recommended for use in combination with methotrexate.
Children and adolescents from 2 years of age weighing 30 kg or more	40 mg every other week	Your doctor may prescribe an initial dose of 80 mg to be administered one week prior to the start of the usual dose of 40 mg every other week. Humira is recommended for use in combination with methotrexate.

Method and route of administration

Humira is administered by injection under the skin (by subcutaneous injection).

Detailed instructions on how to inject Humira are provided in section 7 'Injecting Humira'.

If you use more Humira than you should

If you accidentally inject Humira more frequently than told to by your doctor or pharmacist, call your doctor or pharmacist and tell them that you have taken more. Always take the outer carton of the medicine with you, even if it is empty.

If you forget to use Humira

If you forget to give yourself an injection, you should inject the next dose of Humira as soon as you remember. Then take your next dose as you would have on your originally scheduled day, had you not forgotten a dose.

If you stop using Humira

The decision to stop using Humira should be discussed with your doctor. Your symptoms may return if you stop using Humira.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Most side effects are mild to moderate. However, some may be serious and require treatment. Side effects may occur at least up to 4 months after the last Humira injection.

Tell your doctor immediately if you notice any of the following

- severe rash, hives or other signs of allergic reaction
- swollen face, hands, feet
- trouble breathing, swallowing
- shortness of breath with physical activity or upon lying down or swelling of the feet

Tell your doctor as soon as possible if you notice any of the following

- signs of infection such as fever, feeling sick, wounds, dental problems, burning on urination
- feeling weak or tired
- coughing
- tingling
- numbness
- double vision
- arm or leg weakness
- a bump or open sore that doesn't heal
- signs and symptoms suggestive of blood disorders such as persistent fever, bruising, bleeding, paleness

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

Very common (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 infection, pneumonia)
- headache

- abdominal pain
- nausea and vomiting
- rash
- musculoskeletal pain

Common (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)
- ear infections
- oral infections (including tooth infections and cold sores)
- reproductive tract infections
- urinary tract infection
- fungal 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
- migraine
- nerve root compression (including low back pain and leg pain)
- vision disturbances
- eye inflammation
- inflammation of the eye lid and eye swelling
- vertigo (feeling of dizziness or spinning)
- sensation of heart beating rapidly
- high blood pressure
- flushing
- haematoma (collection of blood outside of blood vessels)
- 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 finger nails and toe nails
- increased sweating
- hair loss
- new onset or worsening of psoriasis
- muscle spasms

- blood in urine
- kidney problems
- chest pain
- oedema (swelling)
- fever
- reduction in blood platelets which increases risk of bleeding or bruising
- impaired healing

Uncommon (may affect up to 1 in 100 people)

- opportunistic infections (which include 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
- melanoma
- immune disorders that could affect the lungs, skin and lymph nodes (most commonly presenting as sarcoidosis)
- vasculitis (inflammation of blood vessels)
- tremor (shaking)
- neuropathy (disorder of the nerves)
- stroke
- hearing loss, buzzing
- sensation of heart beating irregularly such as skipped beats
- heart problems that can 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 in swallowing
- facial oedema (swelling of the face)
- gallbladder inflammation, gallbladder stones
- fatty liver
- night sweats
- scar
- abnormal muscle breakdown
- systemic lupus erythematosus (including inflammation of skin, heart, lung, joints and other organ systems)
- sleep interruptions
- impotence
- inflammations

Rare (may affect up to 1 in 1,000 people)

- leukaemia (cancer affecting the blood and bone marrow)

- severe allergic reaction with shock
- multiple sclerosis
- nerve disorders (such as eye 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 (hole in the intestine)
- 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)
- Stevens-Johnson syndrome (early symptoms include malaise, fever, headache and rash)
- facial oedema (swelling of the face) associated with allergic reactions
- erythema multiforme (inflammatory skin rash)
- lupus-like syndrome
- angioedema (localized swelling of the skin)
- lichenoid skin reaction (itchy reddish-purple skin rash)

Not known (frequency cannot be estimated from the available data)

- hepatosplenic T-cell lymphoma (a rare blood cancer that is often fatal)
- Merkel cell carcinoma (a type of skin cancer)
- Kaposi's sarcoma, a rare cancer related to infection with human herpes virus 8. Kaposi's sarcoma most commonly appears as purple lesions on the skin
- liver failure
- worsening of a condition called dermatomyositis (seen as a skin rash accompanying muscle weakness)
- weight gain (for most patients, the weight gain was small)

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

Very common (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
- elevated liver enzymes

Common (may affect up to 1 in 10 people)

- high blood measurements for white blood cells
- low blood measurements for platelets
- increased uric acid in the blood
- abnormal blood measurements for sodium
- low blood measurements for calcium
- low blood measurements for phosphate
- high blood sugar
- high blood measurements for lactate dehydrogenase
- autoantibodies present in the blood
- low blood potassium

Uncommon (may affect up to 1 in 100 people)

- elevated bilirubin measurement (liver blood test)

Rare (may affect up to 1 in 1,000 people)

- low blood measurements for white blood cells, red blood cells and platelet count

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Humira

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

Do not use this medicine after the expiry date stated on the label/blister/carton after EXP.

Store in a refrigerator (2°C – 8°C). Do not freeze.

Keep the pre-filled pen in the outer carton in order to protect from light.

Alternative Storage:

When needed (for example, when you are travelling), a single Humira pre-filled pen may be stored at room temperature (up to 25°C) for a maximum period of 14 days – be sure to protect it from light. Once removed from the refrigerator for room temperature storage, the pen **must be used within 14 days or discarded**, even if it is returned to the refrigerator.

You should record the date when the pen is first removed from refrigerator and the date after which it should be discarded.

Do not throw away any medicines via wastewater or household waste. Ask your doctor or pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Humira contains

The active substance is adalimumab.
The other ingredients are mannitol, polysorbate 80 and water for injections.

This Information is Confidential

What the Humira pre-filled pen looks like and contents of the pack

Humira 80 mg solution for injection in pre-filled pen is supplied as a sterile solution of 80 mg adalimumab dissolved in 0.8 ml solution.

The Humira pre-filled pen is a single-use grey and plum-coloured pen which contains a glass syringe with Humira. There are two caps – one is grey and labelled '1' and the other is plum and labelled '2'. There is a window on each side of the pen through which you can see the Humira solution inside the syringe.

The Humira pre-filled pen is available in packs containing:
- 1 pre-filled pen for patient use with 2 alcohol pads (1 spare)
- 3 pre-filled pens for patient use with 4 alcohol pads (1 spare)

Not all pack sizes may be marketed.

Humira may be available as a vial, a pre-filled syringe and/or a pre-filled pen.

Marketing Authorisation Holder

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

Manufacturer

AbbVie Biotechnology GmbH
Knollstrasse
67061 Ludwigshafen
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
AbbVie SA
Tél/Tel: +32 10 477811

България
АбВи ЕООД
Тел.:+359 2 90 30 430

Česká republika
AbbVie s.r.o.
Tel: +420 233 098 111

Danmark
AbbVie A/S
Tlf: +45 72 30-20-28

Deutschland
AbbVie Deutschland GmbH & Co. KG
Tel: 00800 222843 33 (gebührenfrei)
Tel: +49 (0) 611 / 1720-0

Lietuva
AbbVie UAB
Tel: +370 5 205 3023

Luxembourg/Luxemburg
AbbVie SA
Belgique/Belgien
Tél/Tel: +32 10 477811

Magyarország
AbbVie Kft.
Tel.:+36 1 455 8600

Malta
V.J.Salomone Pharma Limited
Tel: +356 22983201

Nederland
AbbVie B.V.
Tel: +31 (0)88 322 2843

Eesti
AbbVie OÜ
Tel: +372 623 1011
Ελλάδα
AbbVie ΦΑΡΜΑΚΕΥΤΙΚΗ Α.Ε.
Τηλ: +30 214 4165 555

España
AbbVie Spain, S.L.U.
Tel: +34 91 384 09 10
France
AbbVie
Tél: +33 (0) 1 45 60 13 00
Hrvatska
AbbVie d.o.o.
Tel + 385 (0)1 5625 501
Ireland
AbbVie Limited
Tel: +353 (0)1 4287900
Ísland
Vistor hf.
Tel: +354 535 7000
Italia
AbbVie S.r.l.
Tel: +39 06 928921
Κύπρος
Lifepharma (Z.A.M.) Ltd
Τηλ.: +357 22 34 74 40
Latvija
AbbVie SIA
Tel: +371 67605000

Norge
AbbVie AS
Tlf: +47 67 81 80 00
Österreich
AbbVie GmbH
Tel: +43 1 20589-0

Polska
AbbVie Polska Sp. z o.o.
Tel.: +48 22 372 78 00
Portugal
AbbVie, Lda.
Tel: +351 (0)21 1908400
România
AbbVie S.R.L.
Tel: +40 21 529 30 35
Slovenija
AbbVie Biofarmacevtska družba d.o.o.
Tel: +386 (1)32 08 060
Slovenská republika
AbbVie s.r.o.
Tel: +421 2 5050 0777
Suomi/Finland
AbbVie Oy
Puh/Tel: +358 (0)10 2411 200
Sverige
AbbVie AB
Tel: +46 (0)8 684 44 600
United Kingdom (Northern Ireland)
AbbVie Deutschland GmbH & Co. KG
Tel: +44 (0)1628 561090

This leaflet was last revised in

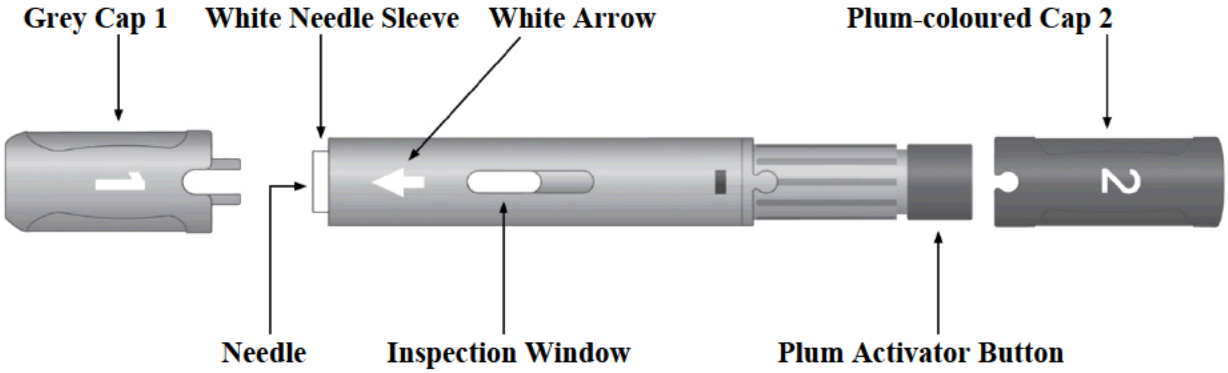
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

To listen to or request a copy of this leaflet in <Braille>, <large print> or <audio>, please contact the local representative of the Marketing Authorisation Holder.

7. Injecting Humira

- The following instructions explain how to give yourself a subcutaneous injection of Humira using the pre-filled pen. First read all the instructions carefully and then follow them step by step.
- You will be instructed by your doctor, nurse or pharmacist on the technique of self-injection.
- Do not attempt to self-inject until you are sure that you understand how to prepare and give the injection.
- After proper training, the injection can be given by yourself or given by another person, for example, a family member or friend.
- Only use each pre-filled pen for one injection.

Humira Pre-filled Pen



Do not use the pre-filled pen and call your doctor or pharmacist if the

- liquid is cloudy, discoloured, or has flakes or particles in it
- expiry (EXP) date has passed
- liquid has been frozen or left in direct sunlight
- pre-filled pen has been dropped or crushed

Do not remove the caps until just before injection. Keep Humira out of the sight and reach of children.

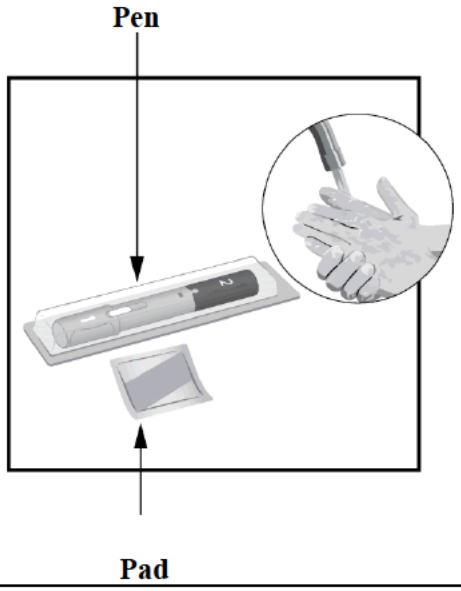
STEP 1

Take Humira out of the refrigerator.

Leave Humira at room temperature for **15 to 30 minutes** before injecting.

- **Do not** remove the Grey or Plum-coloured Caps while allowing Humira to reach room temperature
- **Do not** warm Humira in any other way. For example, **do not** warm it in a microwave or in hot water

STEP 2



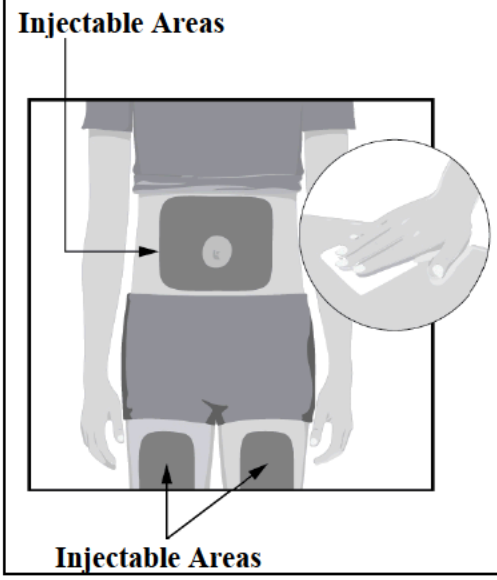
Check expiry (EXP) date. **Do not** use the pre-filled pen if expiry (EXP) date has passed.

Place the following on a clean, flat surface

- 1 single-use pre-filled pen and
- 1 alcohol pad

Wash and dry your hands.

STEP 3



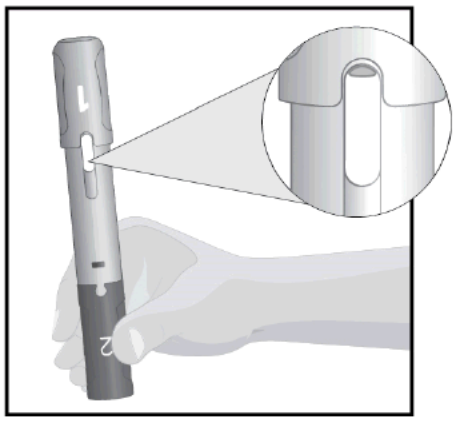
Choose an injection site:

- On the front of your thighs or
- Your belly (abdomen) at least 5 cm from your belly button (navel)
- At least 3 cm from your last injection site

Wipe the injection site in a circular motion with the alcohol pad.

- **Do not** inject through clothes
- **Do not** inject into skin that is sore, bruised, red, hard, scarred, has stretch marks, or areas with psoriasis plaques

STEP 4



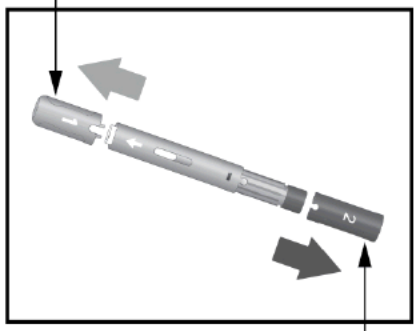
Hold the pre-filled pen with the Grey Cap 1 pointing up.

Check the inspection window.

- It is normal to see 1 or more bubbles in the window
- Make sure the liquid is clear and colourless
- **Do not** use the pre-filled pen if the liquid is cloudy or has particles
- **Do not** use the pre-filled pen if it has been dropped or crushed

STEP 5

Cap 1



Cap 2

Pull the Grey Cap 1 straight off. Throw the cap away. **Do not** recap.

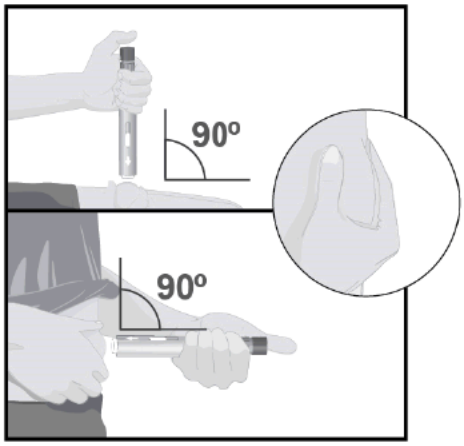
- Check that the small black needle cover of the syringe has been removed with the cap
- It is normal to see a few drops of liquid come out of the needle

Pull the Plum-coloured Cap 2 straight off. Throw the cap away. **Do not** recap.

The pre-filled pen is now ready to use.

Turn the pre-filled pen so that the white arrow points toward the injection site.

STEP 6



Squeeze the skin at your injection site with your other hand to make a raised area and hold it firmly until the injection is complete.

Point the white arrow toward the injection site (thigh or abdomen).

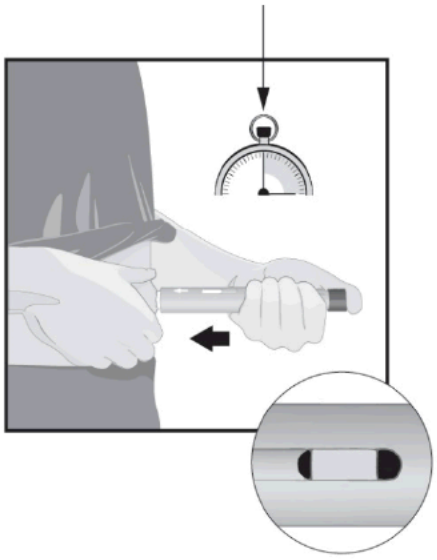
Place the white needle sleeve straight **(90° angle)** against the injection site.

Hold the pre-filled pen so that you can see the inspection window.

Do not press the plum activator button until you are ready to inject.

STEP 7

15 Seconds



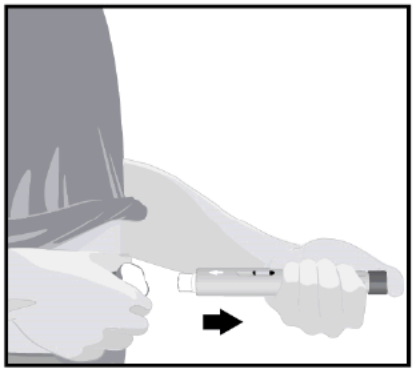
Firmly push the pre-filled pen down against the injection site before starting the injection.
Keep pushing down to prevent the pre-filled pen from moving away from the skin during the injection.

Press the plum activator button and count slowly for **15** seconds.

- A loud **"click"** will signal the start of the injection
- **Keep pushing** the pre-filled pen down **firmly** against the injection site until the injection is complete.

The injection is complete when the yellow indicator has stopped moving.

STEP 8



When the injection is completed, slowly pull the pre-filled pen from the skin. The white needle sleeve will cover the needle tip.

- A small amount of liquid on the injection site is normal

If there are more than a few drops of liquid on the injection site, contact your doctor, nurse or pharmacist.

After completing the injection, place a cotton ball or gauze pad on the skin over the injection site.

- **Do not** rub
- Slight bleeding at the injection site is normal

STEP 9

Throw away the used pre-filled pen in a special disposal container as instructed by your doctor, nurse or pharmacist.

- **Do not** recycle or throw the pre-filled pen in the household waste
- **Always** keep the pre-filled pen and the special disposal container out of the sight and reach of children

The caps, alcohol pad, cotton ball or gauze pad, blister and packaging may be put in your household waste.

Humira 40 mg solution for injection in pre-filled syringe（和文）

Humira 40 mg solution for injection in pre-filled pen（和文）

1. 製品名

Humira 40 mg 注射液プレフィルドシリンジ
Humira 40 mg 注射液プレフィルドペン

2. 組成及び含量

Humira 40 mg 注射液プレフィルドシリンジ
0.4 mL の単回投与用プレフィルドペン中に 40 mg のアダリムマブを含む。

Humira 40 mg 注射液オートマチックニードルガード付きプレフィルドシリンジ
0.4 mL の単回投与用プレフィルドペン中に 40 mg のアダリムマブを含む。

Humira 40 mg 注射液プレフィルドペン
0.4 mL の単回投与用プレフィルドシリンジ中に 40 mg のアダリムマブを含む。

アダリムマブは，チャイニーズハムスター卵巣細胞で作製された組換えヒトモノクローナル抗体である。

添加物は，6.1 参照。

3. 剤型

注射用液（注射剤）
無色澄明な液剤

4. 臨床的特徴

4.1 適応症

関節リウマチ
MTX と Humira の併用において，

- MTX を含む DMARDs の効果が不十分な中等症から重症の活動性関節リウマチの成人患者に対する治療。
- MTX の治療歴のない重症の活動性及び進行性関節リウマチの成人患者に対する治療。

MTX 不耐容の場合，又は MTX 治療の継続が適切でない場合，Humira を単独投与する。

Humira は，MTX との併用において，X 線検査により測定される関節の構造的損傷の進展抑制及び身体機能の改善がみられた。

若年性特発性関節炎
多関節型若年性特発性関節炎
MTX との併用において，1 剤以上の DMARDs の効果不十分な，活動性多関節型若年性特発性関節炎の 2 歳以上の患者に対する治療。MTX 不耐容の場合又は MTX の治療継続が適切でない場合，Humira を単独投与する（単独投与の有効性は，5.1 参照）。2 歳未満の小児を対象とした試験は行われていない。

腱付着部炎関連関節炎
通常の治療法で効果不十分，又は不耐容である活動性腱付着部炎関連関節炎の 6 歳以上の患者に対する治療（5.1 参照）。

体軸性脊椎関節炎
強直性脊椎炎(AS)
通常の治療法の効果が不十分な重症の活動性強直性脊椎炎の成人患者に対する治療。

AS の証拠となる X 線像が認められない体軸性脊椎関節炎

Humira は，非ステロイド性抗炎症薬（NSAIDs）で十分な効果が得られなかった又は不耐容であった，AS の証拠となる X 線像は認められず，CRP の上昇及び/又は MRI により炎症の客観的兆候が認められる重症の体軸性脊椎関節炎の成人の治療に適応される。

関節症性乾癬
DMARDs の効果が不十分な，活動性及び進行性の関節症性乾癬の成人患者に対する治療。Humira 投与により，対称性多関節型（5.1 参照）の患者において X 線検査により末梢関節の構造的損傷の進展抑制及び身体機能の改善がみられた。

乾癬
全身療法の対象となる中等症から重症の慢性尋常性乾癬の成人患者に対する治療。

小児尋常性乾癬
局所療法及び光線療法で効果不十分，又は適切でない場合の重度の慢性尋常性乾癬を有する小児及び 4 歳以上の若年患者に対する治療。

化膿性汗腺炎
従来の全身療法（5.1 及び 5.2 参照）では十分な効果が得られない中等症から重症の活動性化膿性汗腺炎の成人及び 12 歳以上の患者に対する治療。

クローン病
副腎皮質ステロイド／免疫抑制剤による治療の効果が不十分又はこの治療に不耐容又は禁忌である重症の活動性クローン病患者に対する治療。

小児クローン病
一次栄養療法，副腎皮質ステロイド及び／若しくは免疫調節薬を含む通常の治療法で効果不十分，又はこれらの治療に不耐容又は禁忌である中等度から重症の活動性クローン病の小児患者（6 歳以上）に対する治療。

潰瘍性大腸炎
副腎皮質ステロイド，6-メルカプトプリン又はアザチオプリンを含む通常の治療法で効果不十分，又はこの治療に不耐容又は禁忌である中等症から重症の活動性潰瘍性大腸炎の成人患者に対する治療。

小児潰瘍性大腸炎
副腎皮質ステロイド，6-メルカプトプリン又はアザチオプリンを含む通常の治療法で効果不十分，又はこの治療に不耐容又は禁忌である中等症から重症の活動性潰瘍性大腸炎の小児患者（6 歳以上）に対する治療。

ぶどう膜炎
副腎皮質ステロイドで効果不十分，副腎皮質ステロイドの減量を必要とする，又は副腎皮質ステロイドによる治療が不適切な非感染性中間部，後部及び汎ぶどう膜炎の成人患者に対する治療。

小児ぶどう膜炎
通常の治療法で効果不十分若しくは不耐容である，又は通常の治療法が不適切な，2 歳以上の小児慢性非感染性前部ぶどう膜炎患者に対する治療。

4.2 用法・用量

Humira による治療は，Humira 適応症の診断と治療に経験のある専門の医師の監視下で開始すること。眼科医は Humira の治療開始前に適切な専門医から助言を受けることが推奨される（4.4 参照）。Humira で治療する患者は特別な患者リマインダーカードが与えられる。

注射技術についての適切なトレーニング後，適切であると医師が判断した患者については，必要に応じて医学的なフォローアップを行いながら Humira を自己投与できる。

Humira 投与中，併用療法（例えば，副腎皮質ステロイド／免疫調節剤）を考慮すること。

用量

関節リウマチ
関節リウマチの成人患者に対する Humira の推奨用量は，アダリムマブ 40 mg の皮下注射による隔週投与。MTX は Humira の治療中も継続すること。

副腎皮質ステロイド，サリチル酸塩，NSAIDs 又は鎮痛剤は Humira による治療中も継続可能。MTX 以外の DMARDs との併用に関しては，4.4 及び 5.1 参照。

単独療法において，Humira 40 mg の隔週投与で効果の減弱を経験した患者については，アダリムマブ 40 mg の週 1 回投与又は 80 mg の隔週投与へ用量を増量することにより効果を得られる可能性がある。

上述の適応症に関しては，通常，治療 12 週間以内に臨床的効果が得られる。この期間に反応が得られなかった患者においては，治療の継続を再検討すべきである。

各患者の治療ニーズに応じて別の含量や剤形を使用してもよい。

投与中断
例えば手術前又は重篤な感染症が発現した場合は，投与中断が必要なことがある。

70 日間以上の投与中断後，Humira の再投与により，投与中断前と同程度の臨床的効果及び同様の安全性プロファイルが得られた。

強直性脊椎炎，AS の証拠となる X 線像が認められない体軸性脊椎関節炎及び関節症性乾癬
強直性脊椎炎，AS の証拠となる X 線像が認められない体軸性脊椎関節炎及び関節症性乾癬の患者に対する Humira の推奨用量は，アダリムマブ 40 mg の隔週単回皮下注射である。

上述の適応症に関しては，通常，治療 12 週間以内に臨床的効果が得られる。この期間に反応が得られなかった患者においては，治療の継続を注意深く再検討すべきである。

乾癬
成人患者に対する推奨用量は，初回 80 mg，初回投与後 1 週時より 40 mg の皮下注射による隔週投与。

16 週間以内に効果が得られなかった患者においては，治療の継続を慎重に再検討すること。

16 週間以降，Humira 40 mg 隔週投与において反応が不十分な患者でも用量を 40 mg 毎週投与又は 80 mg 隔週投与に増量することにより効果が得られる可能性はある。用量を増量しても応答が不十分な患者に対しては，40 mg 毎週投与又は 80 mg 隔週投与の継続の効果とリスクを注意深く再検討すべきである（5.1 参照）。40 mg 毎週投与又は 80 mg 隔週投与で十分な反応が達成される場合，その後 40 mg 隔週投与に減量することも可能である。

各患者の治療ニーズに応じて別の含量や剤形を使用してもよい。

化膿性汗腺炎

化膿性汗腺炎の成人患者に対する Humira の推奨投与レジメンは，初回（1 日目）に 160 mg（1 日に 40 mg を 4 回，又は 1 日に 40 mg を 2 回連続 2 日間），2 週間後（15 日目）に 80 mg（1 日に 40 mg を 2 回投与）を投与し，その 2 週間後（29 日目）以降は 40 mg 毎週投与又は 80 mg 隔週投与（1 日に 40 mg を 2 回投与）を継続する，である。必要に応じて，Humira の治療中に抗生物質を継続投与することも可能である。患者には，Humira の治療中に毎日患部を消毒薬で洗浄すること。

12 週間の期間内に改善がみなれない患者に対しては，その期間を超える継続療法を注意深く再考慮する必要がある。

治療が中断された場合でも，Humira 40 mg の毎週投与又は 80 mg の隔週投与を再開することができる（5.1 参照）。

継続長期投与の効果とリスクは周期的に評価する必要がある（5.1 参照）。

各患者の治療ニーズに応じて別の含量や剤形を使用してもよい。

クローン病

中等症から重症の活動性クローン病成人患者に対する導入用量は，0 週時で 80 mg 続いて 2 週時で 40 mg 投与。より速やかな効果が必要な場合，導入期間中に有害事象のリスクが高まることを考慮の上，0 週時で 160 mg（1 日に 40 mg を 4 回，又は 1 日に 40 mg を 2 回連続 2 日間），続いて 2 週時で 80 mg（1 日に 40 mg を 2 回投与）投与が可能である。

導入療法後，推奨用量は隔週 40 mg 皮下投与。患者が Humira の投与を中止し，疾患の徴候や症状が再発した場合，Humira を再度投与できる。前回の投与から 8 週間以上経過後の再投与の報告はほとんどない。

維持療法期間中，標準的治療法ガイドラインに従い，副腎皮質ステロイドの投与量を徐々に減らすことができる。

Humira 40 mg 隔週投与において効果が減弱した患者では，Humira 40 mg 毎週投与又は 80 mg 隔週投与へ用量を増量することにより，効果を得られる可能性がある。

4 週時までに効果が現れない患者は，12 週時まで維持療法の継続により，効果が得られる可能性がある。この時期まで効果が得られない患者に対する継続投与については，慎重に再検討すること。

各患者の治療ニーズに応じて別の含量や剤形を使用してもよい。

潰瘍性大腸炎

中等症から重症の潰瘍性大腸炎成人患者に対する導入用量は，0 週時で 160 mg（1 日に 40 mg を 4 回，又は 1 日に 40 mg を 2 回連続 2 日間）及び 2 週時で 80 mg 投与（1 日に 40 mg を 2 回投与）。導入療法後，推奨用量は隔週 40 mg 皮下投与。

維持療法期間中，標準的治療法ガイドラインに従い，副腎皮質ステロイドの投与量を徐々に減らすことができる。

40 mg 隔週投与において効果が減弱した患者では，Humira 40 mg 毎週投与又は 80 mg 隔週投与へ用量を増量することにより，効果を得られる可能性がある。

通常，治療 2–8 週間以内に臨床的効果が得られることを示唆するデータはある。この時期に効果が得られない患者においては，治療を継続しないこと。

各患者の治療ニーズに応じて別の含量や剤形を使用してもよい。

ぶどう膜炎

ぶどう膜炎成人患者への Humira の推奨用量は，初回 80 mg，その後，初回投与の 1 週間後から 40 mg 隔週投与。Humira を単剤で使用して治療を開始する経験は限られている。Humira による治療は副腎皮質ステロイド及び/又は，その他の非生物学的免疫調節薬との併用で開始することができる。併用する副腎皮質ステロイドは，Humira 治療開始の 2 週間以降の臨床診療の結果をふまえて，投与量の漸減を行う場合がある。

長期治療の継続のベネフィット及びリスクを年に一度，評価することが推奨される（5.1 参照）。

各患者の治療ニーズに応じて別の含量や剤形を使用してもよい。

特別な患者集団

高齢者
用量の調整は必要とされてない。

腎及び肝機能障害
Humira はこれらの患者を対象にした試験を行っていない。推奨される用量はない。

小児
若年性特発性関節炎
多関節型若年性特発性関節炎（2 歳以上）
2 歳以上の多関節型若年性特発性関節炎患者に対する推奨用量は，体重に基づいて適用する（表 1）。皮下注射による隔週投与。

表 1.　　多関節型若年性特発性関節炎に対する用法・用量

患者の体重	用法
10–30 kg 未満	20 mg 隔週投与
30 kg 以上	40 mg 隔週投与

通常，治療 12 週間以内に臨床的効果が得られる。この時期まで効果が得られない患者においては，治療の継続を慎重に再検討すること。

本適応症について，2 歳未満の患者に対する Humira の使用経験はない。

各患者の治療ニーズに応じて別の含量や剤形を使用してもよい。

腱付着部炎関連関節炎
6 歳以上の腱付着部炎関連関節炎患者に対する推奨用量は，体重に基づいて適用する（表 2）。皮下注射による隔週投与。

表 2.　　腱付着部炎関連関節炎に対する用法・用量

患者の体重	用法
15–30 kg 未満	20 mg 隔週投与
30 kg 以上	40 mg 隔週投与

Humira は 6 歳未満の腱付着部炎関連関節炎患者を対象にした試験を行っていない。

各患者の治療ニーズに応じて別の含量や剤形を使用してもよい。

関節症性乾癬及び強直性脊椎炎を含む体軸性脊椎関節炎
本適応症（強直性脊椎炎及び関節症性乾癬）について，小児に対する Humira の使用経験はない。

小児尋常性乾癬
4 歳から 17 歳までの尋常性乾癬患者に対する推奨用量は，体重に基づいて適用する（表 3）。皮下注射による投与。

表 3.　　小児尋常性乾癬に対する用法・用量

患者の体重	用法
15–30 kg 未満	20 mg で初回投与し，続いて初回投与の 1 週間後より 20 mg を隔週投与
30 kg 以上	40 mg で初回投与し，続いて初回投与の 1 週間後より 40 mg を隔週投与

16 週以内に効果が得られない患者に対する継続投与については慎重に検討すること。

Humira の再治療が検討された場合は，用量および治療期間に関する上記ガイダンスに従うこと。

Humira の尋常性乾癬の小児患者における安全性を 13 ヵ月間評価した。

本適応症について，4 歳未満の小児に対する Humira の使用経験はない。

各患者の治療ニーズに応じて別の含量や剤形を使用してもよい。

若年性化膿性汗腺炎（12 歳以上，最低体重 30 kg 以上）

Humira の臨床試験における若年性患者の化膿性汗腺炎は実施されていない。
これらの患者に対する用法・用量は薬物動態のモデリング及びシミュレーションにおいて決められている（5.2 参照）。

Humira の推奨導入用量は，0 週時で 80 mg，続いて 40 mg を隔週で 1 週時より皮下投与。各患者の治療ニーズに応じて別の含量や剤形を使用してもよい。

Humira 40 mg の隔週投与において効果不十分な若年性患者には用量を 40 mg 毎週投与又は 80 mg 隔週投与に増量することを検討する。

必要に応じて，Humira 治療中に抗生物質を継続する。
Humira 治療中は，毎日局所用消毒剤の洗浄液を使用することを推奨する。

12 週間以上で効果が現れない患者に対する継続投与については，注意深く再考されるべきである。治療が中断された場合，適切に Humira の投与を再検討する。

継続的な長期治療のリスク／ベネフィットは，定期的に評価されるべきである（5.1 成人のデータ参照）。本適応症について，12 歳未満の小児に対する Humira の使用経験はない。

各患者の治療ニーズに応じて別の含量や剤形を使用してもよい。

小児クローン病
6 歳から 17 歳までの小児クローン病患者に対する推奨用量は，体重に基づいて適用する（表 4）。皮下注射による投与。

表 4.　　小児クローン病に対する用法・用量

患者の体重	導入用量	4 週時以降の維持用量
40 kg 未満	• 0 週時に 40 mg，2 週時に 20 mg より高い導入用量を用いて有害事象のリスクが高まる可能性があることを考慮した上で，より速やかな効果が必要な場合，以下の用量での投与が可能である。 • 0 週時に 80 mg，2 週時に 40 mg	20 mg 隔週投与
40 kg 以上	• 0 週時に 80 mg，2 週時に 40 mg より高い導入用量を用いて有害事象のリスクが高まる可能性があることを考慮した上で，より速やかな効果が必要な場合，以下の用量での投与が可能である。 • 0 週時に 160 mg，2 週時に 80 mg	40 mg 隔週投与

十分な効果が得られない患者では，Humira の用量を増量することにより，効果を得られる可能性がある。

- 40 kg 未満：20 mg 週 1 回投与
- 40 kg 以上：40 mg 週 1 回投与又は 80 mg 隔週投与

12 週時までに効果が現れない患者に対する継続投与については，慎重に検討すること。

本適応症について，6 歳未満の小児に対する Humira の使用経験はない。

各患者の治療ニーズに応じて別の含量や剤形を使用してもよい。

小児潰瘍性大腸炎

6 歳から 17 歳までの潰瘍性大腸炎患者に対する推奨用量は，体重に基づいて適用する（表 5）。皮下注射による投与。

表 5.　　小児潰瘍性大腸炎に対する用法・用量

患者の体重	導入用量	4 週時以降*の維持用量
40 kg 未満	• 0 週時に 80 mg（1 日に 40 mg を 2 回投与） • 2 週時に 40 mg（1 日に 40 mg を 1 回投与）	40 mg 隔週投与
40 kg 以上	• 0 週時に 160 mg（1 日に 40 mg を 4 回，又は 1 日に 40 mg を 2 回連続 2 日間投与） • 2 週時に 80 mg（1 日に 40 mg を 2 回投与）	80 mg 隔週投与

* Humira 投与中に 18 歳に達した小児患者においては維持用量の処方を継続すること。

8 週間以内に効果の徴候を示さなかった患者に対する継続投与については，慎重に検討すること。

本適応症について，6 歳未満の小児に対する Humira の使用経験はない。

各患者の治療ニーズに応じて別の含量や剤形を使用してもよい。

小児ぶどう膜炎

ぶどう膜炎を有する 2 歳以上の小児患者に対する推奨用量は，体重に基づいて適用する（表 6）。皮下注射による投与。

小児ぶどう膜炎に対して，メトトレキサートを併用せずに Humira を使用した経験はない。

表 6.　　小児ぶどう膜炎に対する用法・用量

患者の体重	用法
30 kg 未満	メトトレキサート併用下で 20 mg 隔週投与
30 kg 以上	メトトレキサート併用下で 40 mg 隔週投与

Humira の投与開始時には，場合により，30 kg 未満の患者には 40 mg，30 kg 以上の小児には 80 mg を用いて，維持療法を始める 1 週間前に負荷投与を行うこととする。6 歳未満の小児に対する Humira の負荷投与に関する利用可能な臨床データは得られてない（5.2 参照）。

本適応症について，2 歳未満の小児に対する Humira の使用経験はない。

長期治療の継続のベネフィット及びリスクを年に一度，評価することが推奨される（5.1 参照）。

各患者の治療ニーズに応じて別の含量や剤形を使用してもよい。

用法
Humira は皮下投与する。使用上の注意の詳細は添付文書に記載する。

Humira は，上記以外の含量や剤形で使用することができる。

4.3 禁忌

主成分若しくは 6.1 に記載されている添加物のいずれかに過敏症がある患者

活動性結核若しくは，敗血症等その他の重篤な感染症及び日和見感染症の患者（4.4 参照）

中等症から重症の心不全患者（NYHA クラス III/IV）（4.4 参照）

4.4 特別な警告と使用上の注意

トレーサビリティ
生物学的医薬品のトレーサビリティを向上させるため，投与した薬剤名及びロット番号を明確に記録すること。

感染症
TNF 拮抗薬を投与している患者において重篤な感染症により感染しやすくなる。肺機能障害は感染症の発症リスクを増加する可能性がある。Humira による治療前，治療中及び治療後に，結核を含む感染症について注意深く観察すること。アダリムマブの体内からの消失には，最高 4 ヵ月かかる可能性があるため，観察はこの期間中続けること。

感染症が抑えられるまで慢性若しくは局所的な感染症を含む活動性の感染症の患者に対して Humira による治療は開始しないこと。結核に曝露された患者及び結核又はヒストプラスマ症，コクシジオイデス症又はブラストミセス症などの流行性の真菌症の危険性の高い地域へ旅行したことのある患者については，Humira による治療のリスク／ベネフィットを治療開始前に検討すること（日和見感染症参照）。

Humira による治療中に新たな感染症が発現した患者に対して，注意深く観察し，診断的評価を行うこと。新たな重篤な感染症又は敗血症が生じた患者は，Humira の投与を中止し，感染症が抑えられるまで適切な抗菌薬又は抗真菌薬治療を行うこと。再発性感染症の既往がある又は

感染症に罹りやすくなる可能性のある基礎疾患を有する患者，免疫抑制剤併用の場合は，Humira の使用を検討する際に医師は注意すること。

重篤な感染症：
Humira を投与している患者において，敗血症，細菌，マイコバクテリア，侵襲性真菌，寄生虫，ウイルスによる感染症又はリステリア症，レジオネラ症及びニューモシスティスなどの他の日和見感染症を含む重篤な感染症が報告されている。

臨床試験でみられた他の重篤な感染症は，肺炎，腎盂腎炎，敗血症性関節炎及び敗血症。入院又は致死的な感染症が報告されている。

結核：
Humira による治療を行っている患者において結核の報告がある。これらの報告の多くは，播種性などの肺外結核であった。

Humira による治療の開始前に，全ての患者は活動性若しくは非活動性（潜在性）の結核感染か評価する。この評価には，詳細な治療歴，結核の既往歴，過去に活動性の結核患者及び過去／現在免疫抑制剤の治療を受けている患者への接触の可能性を含めること。
適切なスクリーニングテスト，ツベルクリン反応検査及び胸部 X 線は全ての患者で行うこと（現地の推奨方法を適用する）。これらの検査を行うことを患者リマインダーカードに記録することを勧める。処方者は，特に重篤な疾病，免疫力がない患者には，偽陰性のツベルクリン反応検査結果のリスクについて注意を促す。

活動性の結核と診断された場合，Humira の治療は開始しない（4.3 参照）。

潜在性の結核が疑われる場合，結核治療の経験のある医師と相談すること。下記に記載した全ての場合，Humira の治療のベネフィット／リスクのバランスを注意深く検討すること。

非活動性（潜在性）の結核と診断された場合，Humira による治療を開始する前に，現地の推奨方法に従い，抗結核薬の予防治療による潜在性結核に適切な治療を行うこと。

結核の種々の又は重大な危険因子を有する患者及び潜在性結核陰性の患者は Humira による治療開始前に抗結核薬の治療を検討すること。

適切な一連の治療が確認できなかった潜在性結核又は活動性結核の既往歴のある患者については，Humira 投与の前に抗結核薬の治療を検討すること。過去に潜在性若しくは活動性結核の治療を受けた患者は，Humira 投与中に活動性結核を発現することがある。

Humira による治療中又は治療後，もし結核感染を示唆する徴候／症状（例 持続性の咳，消耗／体重の減少，微熱）が現れた場合，患者には医学的なアドバイスを求めるよう指示すること。

その他の日和見感染症：
Humira を投与している患者において，侵襲性真菌感染症を含む日和見感染症が認められている。これらの感染症は TNF 拮抗薬を投与している患者において常にみられるものではなく，そのため適切な治療の遅れを招き，致死的な結果をもたらすこともある。

発熱，不快感，体重減少，発汗，咳，呼吸困難，及び／又は肺浸潤又はショックを伴う如何に関わらず他の重篤な全身疾患などの徴候及び症状がみられた患者に関しては，侵襲性真菌感染症を疑い，Humira の投与は直ちに中止すること。これらの患者に対する診断及び抗真菌薬の経験的投与は，侵襲性真菌感染症患者治療の専門である医師に相談すること。

B 型肝炎の再燃
Humira を含む TNF 拮抗薬の投与を受けている B 型肝炎ウイルス慢性キャリア患者（表面抗原陽性）において，B 型肝炎の再燃が認められている。致死的な例も報告されている。Humira の投与に先立ち，HBV 感染の検査をすること。B 型肝炎感染陽性患者は，B 型肝炎の治療における専門の医師と相談することが望ましい。

Humira による治療が必要な HBV キャリア患者は，投与中のみならず，投与終了後も数ヵ月は活動性 HBV 感染の徴候及び症状を十分に観察すること。HBV キャリア患者に対する再燃予防のための抗ウイルス薬治療と TNF 拮抗薬治療との併用における十分なデータは得られていない。HBV が再燃した患者は Humira の投与を中止し，有効な抗ウイルス療法等適切な処置を開始すること。

神経症状
Humira を含む TNF 拮抗薬は，まれに多発性硬化症を含む中枢神経系脱髄疾患及びギラン・バレー症候群を含む末梢脱髄疾患の臨床症状／放射線診断による新たな発生若しくは悪化に関連する。処方者は，既往又は最近発症した中枢又は末梢神経系脱髄疾患の患者に Humira を使用させる場合は注意すること。これらの疾患のいずれかが現れた場合は Humira の使用中止を検討すべきである。中間部ぶどう膜炎と中枢神経系脱髄性疾患には関連性があることが分かっている。以前から存在している又は最近発症した中枢神経系脱髄性疾患の有無を評価するために，非感染性中間部ブドウ膜炎に罹患する患者に対して Humira 治療の開始前と治療中，定期的に神経学的評価を実施すべきである。

アレルギー反応

臨床試験中に認められた，Humira に関連する重篤なアレルギー反応はまれであった。Humira に関連する重篤でないアレルギー反応は，臨床試験中にまれに認められた。Humira 投与後に発現したアナフィラキシーを含む重篤なアレルギー反応が報告されている。アナフィラキシー反応若しくは他の重篤なアレルギー反応が生じた場合，Humira の投与は直ちに中止し，適切な治療を開始すること。

免疫低下

Humira を投与された関節リウマチ患者 64 例における試験で，遅発性過敏症の抑制，免疫グロブリン濃度の低下，エフェクターT 細胞と B 細胞及び NK 細胞，単球／マクロファージ，好中球の変化を示す徴候は認められなかった。

悪性腫瘍及びリンパ増殖性疾患

TNF 拮抗薬の比較対照試験において，対照群の患者に比べ，TNF 拮抗薬を投与した患者において多くのリンパ腫を含む悪性腫瘍が認められているが，発現はまれであった。市販後において，TNF 拮抗薬による治療を行った患者で白血病が報告されている。長期にわたる活動性の高い炎症性疾患のある関節リウマチ患者では，リンパ腫及び白血病のリスクは増加し，炎症性疾患はリスク予測を複雑にしている。現在の知見では，TNF 拮抗薬で治療している患者において，リンパ腫，白血病及び他の悪性腫瘍を発症するリスクの可能性を除くことはできない。

市販後では，アダリムマブを含む TNF 拮抗薬による治療を行った小児及び 22 歳以下の若年成人の患者（治療開始は 18 歳以下）において，悪性腫瘍が報告され，致死的な例も報告されている。報告の約半数はリンパ腫だった。その他の報告は，さまざまな異なる悪性腫瘍で，免疫抑制と関連しているまれにみられる悪性腫瘍が含まれていた。TNF 拮抗薬による治療を行った小児及び若年成人の悪性腫瘍発症のリスクを除くことはできない。

市販後において，アダリムマブ投与でまれに肝脾 T 細胞リンパ腫が報告されている。この T 細胞リンパ腫は，侵襲性疾患の経過をたどり，通常死に至る。Humira 投与における肝脾 T 細胞リンパ腫には，炎症性腸疾患に対するアザチオプリン又は6-メルカプトプリンとの併用療法を行っていた若年成人患者で発生したものもある。アザチオプリン又は 6-メルカプトプリン及び Humira の併用における潜在的リスクは慎重に考慮されるべきである。Humira による肝脾 T 細胞リンパ腫発生のリスクは除くことはできない（4.8 参照）。

悪性腫瘍の既往患者又は悪性腫瘍を発生した後も Humira による治療を継続している患者を含んだ試験を行っていない。従って，これらの患者に対し Humira による治療を検討する場合は注意すること（4.8 参照）。

全ての患者及び継続して免疫抑制の治療歴のある患者若しくは PUVA 治療歴のある乾癬患者は，Humira 投与前と投与中に非黒色皮膚癌の検査を受けること。アダリムマブを含む TNF 拮抗薬の治療患者で，メラノーマ及びメルケル細胞癌が報告されている（4.8 参照）。

他の TNF 拮抗薬（インフリキシマブ）の使用を評価する探索的臨床試験では，中等症から重症の慢性閉塞性肺疾患（COPD）の患者において，対照群に比べインフリキシマブ投与群で多くの悪性腫瘍（主に肺，頭頸部）が報告されている。全ての患者は高度の喫煙者であった。そのため，高度の喫煙のために悪性腫瘍のリスクが増加した患者だけでなく，COPD 患者で TNF 拮抗薬を投与している場合においても十分注意すること。

現在のデータでは，アダリムマブ治療が異形成や大腸癌を発症するリスクに影響を与えるかどうかは知られていない。異形成や大腸癌を発症するリスクの高い潰瘍性大腸炎のすべての患者（例えば，長期にわたる潰瘍性大腸炎や原発性硬化性胆管炎の患者），又は異形成や大腸癌の既往歴のある潰瘍性大腸炎のすべての患者は，治療前及び疾患の経過中に定期的に異形成のスクリーニングを行うこと。この評価には，その地域の推奨のもとに大腸内視鏡検査及び生検を含めること。

血液学的反応

TNF 拮抗薬で再生不良性貧血を含む汎血球減少症がまれに報告されている。医学的に重要な血球減少症（血小板減少症，白血球減少症等）を含む血液系の有害事象は Humira においても報告されている。Humira 使用中に血液疾患を示唆する徴候及び症状（持続性発熱，あざ，出血，蒼白等）が現れたら，直ちに医師の診察を求めること。重要な血液異常が認められた患者は Humira による治療の中止を検討すること。

ワクチン接種

標準的な 23 株肺炎球菌ワクチン及び 3 種混合インフルエンザウイルスワクチンに対する，類似した抗体反応がアダリムマブ又はプラセボ投与の関節リウマチ成人患者 226 例に観察された。Humira 投与患者で生ワクチンによる二次感染に関するデータは得られていない。

可能であれば，多関節型若年性特発性関節炎の患者において，Humira による治療前に現行の予防接種のガイドラインに従った全ての予防接種を受けることを推奨する。

Humira 投与患者は生ワクチンを除くワクチンを同時に投与してもよい。子宮内でアダリムマブに曝露された乳児への生ワクチン（BCG ワクチンなど）の投与は，母親が妊娠中最後にアダリムマブ投与後 5 ヵ月間は推奨できない。

うっ血性心不全