Temziva

Tocilizumab

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Package leaflet: Information for the patient

Temziva 80mg/4ml concentrate for solution for infusion

Temziva 200mg/10ml concentrate for solution for infusion

Temziva 400mg/20ml concentrate for solution for infusion

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.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed only for you. Do not suggest it to others. It may harm them, even if their signs of illness are the same as yours.
- If you notice any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet?

1. Temziva and its usage
2. What you need to know before you use Temziva
3. Notable items to know before using Temziva
4. Possible side effects
5. How to store Temziva
6. Contents of the pack and other information

1. What Temziva is and what it is used for

Temziva contains the active substance tocilizumab, which is a protein made from specific immune cells (monoclonal antibody), that blocks the action of a specific protein (cytokine) called interleukin-6. IL-6 activity in body causes many symptoms of autoimmune disease such as Rheumatoid Arthritis (RA). Blocking IL-6 receptors can reduce the inflammation in your body and reduce symptoms.

Temziva is used for:

- Treat adults with moderate to severe active rheumatoid arthritis (RA), an autoimmune disease, who have either not responded adequately to, or who were intolerant to, previous therapy with other medicines used for treatment of RA. In this situation Temziva can be given alone or in combination with Methotrexate and other non biologic DMARDs .
- Treat active Systemic Juvenile Idiopathic Arthritis (sJIA) in children aged 2 years and over. Temziva can be given alone or in combination with Methotrexate and other DMARDs.
- Treat active Polyarticular Juvenile Idiopathic Arthritis (pJIA) in children aged 2 years and over. Temziva can be given alone or in combination with Methotrexate.
- Treat Cytokine Release Syndrome (CRS) in adults and children aged 2 years and over. CRS is a side-effect in patients treated with chimeric antigen receptor (CAR) T-cell therapies used to treat certain types of cancer.
- Treat Cytokine Release Syndrome (CRS) in patients with a definite diagnosis of COVID-19.

2. What you need to know before you use Temziva

Do not use Temziva if:

- You are allergic to tocilizumab or any of the other ingredients of this medicine (listed in Section 6)
- You have an active, severe infection.

Warning and precautions:

Talk to your doctor, pharmacist or nurse before you are given Temziva:

- If you have any kind of infection because Temziva may make the existing infection worse. Inform your doctor if you had infection recently or history of chronic infections or had underlying conditions (e.g. diverticulitis, diabetes and interstitial lung disease) which may predispose you to infections. Temziva should not be given in patients with active infections and using of Temziva should be stopped if a serious infection occurs during using Temziva. You should inform your doctor immediately if you have the symptoms of infection such as fever, lethargy, Influenza and etc.
- If you have tuberculosis or previous history of TB, you should inform your doctor. Patients with latent TB should be treated with standard anti-mycobacterial therapy before initiating Temziva. Your doctor will check the signs and symptoms of tuberculosis before starting Temziva. If symptoms of tuberculosis (persistent cough, weight loss, listlessness, mild fever) appear during or after treatment, tell your doctor immediately.
- If you have a history of viral infection like hepatitis B.
- If you have had intestinal ulcers or diverticulitis, you should inform your doctor. Also, in the presence of symptoms such as; abdominal pain, haemorrhage and unexplained changes in bowel habits with the fever which is suggestive for diverticulitis, call you doctor.
- If you experience the allergic reactions such as chest tightness, wheezing, severe dizziness or light-headedness, swelling of the lips or skin rash during treatment with Temziva, you should call your doctor immediately. If such allergic reactions occur, using of Temziva should be stopped immediately and appropriate treatment should be done to reduce the allergy. Also, Temziva should be discontinued permanently.
- If you have a history of liver disease, inform your doctor. Temziva can increase the liver enzymes (particularly when administered concomitantly with MTX) therefore, blood test should be done to evaluate the liver function before starting treatment with Temziva.
- A complete blood count should be performed before starting treatment with Temziva in order to make sure that you have normal levels of white blood cells, neutrophils and platelets. Treatment with Temziva should not be initiated in people who have low levels of white blood cells, neutrophils and platelets.
- If you have high blood level of cholesterol or triglycerides or previous history of it, you should inform your doctor. Measurement of lipid parameters should be performed before and also, 4 to 8 weeks after administration of Temziva. Temziva can disturb lipid profile by increasing the level of these parameters. In this case patients should use the appropriate drugs to regulate lipid profile.
- If you or your close relative have history of central nervous system disease (CNS) such as MS, inform your doctor, because there are some reports that demonstrate the relation between Temziva and CNS disordrs.
- If you have cancer. Your doctor will decide to give you Temziva or not.
- If you have recently been vaccinated (either adult or child), or is planning a vaccination. Live and live attenuated vaccines should not be given concurrently with Temziva. It is highly recommended that all the patients especially elderlies complete the vaccination schedule before starting the treatment.
- If you have cardiovascular risk factors such as increased blood pressure or cholesterol levels. These factors need to be monitored while receiving Temziva.
- If you have moderate to severe kidney function problems, your doctor will monitor you.
- If you have severe persistent headaches.

Children and Adolescents:

Temziva is not recommended in children under 2 years of age because the safety and efficacy of Temziva has not been established in these patient populations.

Other medicines and Temziva:

Tell your doctor if you are taking or have recently taken any medicines even herbal, vitamins and OTC.

Temziva can affect the way some medicines work, and the dose of these may require adjustment. If you are using medicines containing any of the following active substances, tell your doctor:

- methylprednisolone, dexamethasone, used to reduce inflammation
- simvastatin or atorvastatin, used to reduce cholesterol levels
- calcium channel blockers (e.g. amlodipine), used to treat raised blood pressure
- theophylline, used to treat asthma
- warfarin or phenprocoumon, used as a blood thinning agents
- phenytoin, used to treat convulsions
- ciclosporin, used to suppress your immune system during organ transplants
- benzodiazepines, used to relieve anxiety.

Due to lack of clinical experience, Temziva is not recommended for use with other biological medicines for the treatment of RA, sJIA or pJIA.

Pregnancy, Breast-feeding and Fertility:

Pregnancy:

Since there are no adequate data from the use of tocilizumab in pregnant women, Temizva should not be used during pregnancy. Women of childbearing potential must use effective contraception during and up to 3 months after treatment. Tell your doctor if you become pregnant during treatment or in less than 3 month of discontinuation.

Breast-feeding:

It is not known whether Temziva is passed into breast milk. Tell your doctor if you are breast-feeding now. Your doctor will make a decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with Temziva taking into account the benefit of breast-feeding to the child and the benefit of Temziva therapy to the woman.

Fertility:

Available non-clinical data do not suggest an effect on fertility under tocilizumab treatment.

Driving and using machines

Temziva can cause dizziness. If you feel dizzy, do not drive or use machines.

3. How to use Temziva

This medicine is subject to restricted medical prescription by your experienced doctor.

Adult patients with RA

The usual dose of Temziva is 8 mg per kg of body weight, once every four weeks.

For individuals whose body weight is more than 100 kg, doses exceeding 800 mg per infusion are not recommended. Temziva is given through a drip in the vein (intravenous infusion) over one hour.

Children with systemic juvenile idiopathic arthritis (sJIA):

The usual dose of Temziva depends on the weight:

- If the patient weigh less than 30 kg: the dose is **12 mg for every kilogram of body weight.**
- If the patient weigh 30 kg or more: the dose is **8 mg for every kilogram of body weight.**

Children with sJIA will be given Temziva once every 2 weeks through a drip in the vein (intravenous infusion) over one hour.

Children with polyarthritis juvenile idiopathic arthritis (pJIA):

The usual dose of Temziva depends on the weight:

- If the patient weigh less than 30 kg: the dose is **10mg for every kilogram of body weight.**
- If the patient weigh 30 kg or more: the dose is **8 mg for every kilogram of body weight.**

Children with pJIA will be given Temziva once every 4 weeks through a drip in the vein (intravenous infusion) over one hour.

Cytokine Release Syndrome (CRS):

- The usual dose of Temziva is **8 mg for every kg of body weight if patient weigh 30 kg or more.**
- The dose is **12 mg for every kg of body weight if patient weigh less than 30 kg.**

Temziva can be given alone or in combination with corticosteroids.

Special Population

Elderly

No dose adjustment is required in elderly patients >65 years of age.

Renal impairment

No dose adjustment is required in patients with mild renal impairment. Temziva has not been studied in patients with moderate to severe renal impairment. Renal function should be monitored closely in these patients.

Hepatic impairment

Temziva has not been studied in patients with hepatic impairment. Therefore, no dose recommendations can be made.

Recommended dose in children and infants

Temziva is not recommended under age 2.

Method of administration

Temziva is given through a drip in the vein (intravenous infusion) over one hour.

If you miss a dose of Temziva

Since Temziva is given by a doctor or nurse, it is unlikely that you will miss a dose. However, if you are worried, talk to your doctor or nurse.

If you stop being given Temziva

Never stop using your medicine before consulting your physician. In order to take the complete benefit from your medicine, always complete the treatment course recommended by your doctor. If you stop the medicine without your doctor's order, the symptoms of your condition may return. If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible Side Effects

Like other medicines, Temziva may be accompanied with some side effects, although not everybody gets them.

Serious Side effects

Tocilizumab can cause serious side effects. In this case, for performing the best therapeutic actions, you should contact with your doctor immediately.

Serious Infection

Signs of serious infection

- fever and chills
- mouth or skin blisters
- stomach ache

Liver Toxicity

Signs and symptoms of liver toxicity

- tiredness
- abdominal pain
- jaundice (yellow discoloration of skin or eyes)

Allergic reactions during or after infusion:

- difficulty with breathing, chest tightness or light-headedness
- rash, itching, hives, swelling of the lips, tongue or face

Side effects in order to frequency of manifestation:

Very common side effects (may affect more than 1 in 10 people)

- Upper respiratory tract infections with typical symptoms such as cough, blocked nose, runny nose, sore throat and headache
- high blood fat (cholesterol) levels.

Common side effects (may affect up to 1 in 10 people)

- headache
- dizziness
- cough
- shortness of breath
- stomach pain
- mouth ulcers
- rash and itching, hives
- allergic (hypersensitivity) reactions
- fluid retention (oedema) in the lower legs
- high blood pressure
- abnormal liver function (abnormal liver function tests)
- weight increase
- increased bilirubin
- eye infection (conjunctivitis)
- low white blood cell counts shown by blood tests (neutropenia, leucopenia)
- low fibrinogen levels in the blood
- lung infection (pneumonia)
- shingles (herpes zoster)
- cold sores (oral herpes simplex), blisters

Uncommon side effects (may affect up to 1 in 100 people)

- hypothyroidism
- red swollen areas in the mouth
- stomach ulcer
- diverticulitis (fever, nausea, diarrhoea, constipation, stomach pain)
- high blood fat (triglycerides)
- kidney stones

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

- Stevens-Johnson syndrome (skin rash, which may lead to severe blistering and peeling of the skin)
- Fatal Allergic Reactions (Anaphylaxis)
- inflammation of the liver (hepatitis)
- jaundice.

Very rare side effects (may affect up to 1 in every 10,000 people)

- low counts for white blood cells, red blood cells and platelets in blood tests
- liver failure.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

You can report the side effect directly with Food and Drug administration Website, **fda.gov.ir**

5. How to store Temziva

- Keep Temziva out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the label and outer carton after "EXP". The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C - 8°C).
- Do not freeze.
- Keep the vial in the outer carton in order to protect from light.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Temziva contains

The active substance is tocilizumab.

Concentration of Tocilizumab is 20mg/ml in each of the 4,10 and 20ml vials.

The other ingredients are sucrose, polysorbate 80, disodium phosphate dodecahydrate, sodium dihydrogen phosphate dihydrate and water for injections.

What Temziva looks like and contents of the pack

Temziva is a concentrate for solution for infusion.

The concentrate is a clear or pale yellow liquid.

Each pack contains 1 vial of concentrated solution, 1 alcoholic pad and 1 brochure for patient.

Instructions for dilution prior to administration

Temziva is infused intravenously by the doctor or nurse. Drug solution is diluted by sodium chloride 9mg/ml (0.9%) solution for injection and given through a drip in the vein (intravenous infusion) over one hour.

Withdraw a volume of sterile, non-pyrogenic sodium chloride 9 mg/mL (0.9%) solution for injection from a 100 mL infusion bag, equal to the volume of Temziva concentrate required for the patients dose, under aseptic conditions. The required amount of Temziva concentrate should be withdrawn from the vial and placed in the 100 mL infusion bag. This should be a final volume of 100 mL. To mix the solution, gently invert the infusion bag to avoid foaming. In patients weighing less than 30 kg, 50 ml of 0.9% sodium chloride solution for injection is used.

You will be monitored during infusion by doctor or nurse.

Prescribing Temziva in COVID-19

Conditions for prescribing Temziva:

Following the pandemic and according to studies, Temziva can be prescribed in the severe and critical stages of COVID-19 and in Cytokine Release Syndrome caused by this disease.

Accordingly, Temziva can be prescribed in patients with a definite diagnosis of COVID-19 (based on PCR test or imaging results) with any of the following symptoms such as fever above 37 degrees, cough, shortness of breath, breathing more than 30 times per minute, SPO2 level less than or equal to 93%, PaO2/FiO2 ratio less than 300 or Pulmonary involvement.

Warnings:

Make sure you do not have any other serious active infections prior to administrating Temziva. Do not use Temziva in patients with active or latent Tuberculosis, active hepatitis B or C, AIDS and any other immunodeficiencies.

Treatment with Temziva is not recommended in case the ANC is less than 2,000 per cubic millimeter, the platelets are less than 100,000 per cubic millimeter or the liver enzymes level is more than 1.5 times normal.

How to use Temziva in patients with COVID-19:

The recommended dose is 4-8 mg / kg of body weight. (Maximum 800 mg/dose)

In case of worsening symptoms or no improvements, it is possible to prescribe Temziva 12 to 24 hours after the first injection.

How to dilute and prepare Temziva has been explained in" Instructions for dilution prior to administration" part.

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