Package leaflet: Information for the user

Tyenne 20 mg/mL concentrate for solution for infusion
tocilizumab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given 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 or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

In addition to this leaflet, you will be given a **Patient Alert Card,** which contains important safety information that you need to be aware of before and during treatment with Tyenne.

What is in this leaflet

1. What Tyenne is and what it is used for
2. What you need to know before you are given Tyenne
3. How Tyenne is given
4. Possible side effects
5. How to store Tyenne
6. Contents of the pack and other information

1. What Tyenne is and what it is used for

Tyenne 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. This protein is involved in inflammatory processes of the body, and blocking it can reduce the inflammation in your body. Tyenne helps to reduce symptoms such as pain and swelling in your joints and can also improve your performance of daily tasks. Tyenne has been shown to slow the damage to the cartilage and bone of the joints caused by the disease and to improve your ability to do normal daily activities.

- **Tyenne is used to treat adults with moderate to severe active rheumatoid arthritis (RA),** an autoimmune disease, if previous therapies did not work well enough. Tyenne is usually given in combination with methotrexate. However, Tyenne can be given alone if your doctor determines that methotrexate is inappropriate.
- Tyenne can also be used to treat adults who have not had previous methotrexate treatment if they have severe, active and progressive rheumatoid arthritis.
- **Tyenne is used to treat children with sJIA.** Tyenne is used for children aged 2 years and over who have active **systemic juvenile idiopathic arthritis (sJIA),** an inflammatory disease that causes pain and swelling in one or more joints as well as fever and rash. Tyenne is used to improve the symptoms of sJIA and can be given in combination with methotrexate or alone.
- **Tyenne is used to treat children with pJIA.** Tyenne is used for children aged 2 years and over with active **polyarticular juvenile idiopathic arthritis (pJIA),** an inflammatory disease that causes pain and swelling in one or more joints. Tyenne is used to improve the symptoms of pJIA and can be given in combination with methotrexate or alone.
- **Tyenne is used to treat adults and children** aged 2 years and over with severe or life-threatening **cytokine release syndrome** (CRS), a side-effect in patients treated with chimeric antigen receptor (CAR) T-cell therapies used to treat certain types of cancer.
- **Tyenne is used to treat adults with coronavirus disease 2019 (COVID-19),** receiving systemic corticosteroids and requiring supplemental oxygen or mechanical ventilation.

2. What you need to know before you are given Tyenne

Tyenne must not be given
- if you are allergic to tocilizumab or any of the other ingredients of this medicine (listed in section 6).
- if you have an active, severe infection.

If any of these applies to you, tell the doctor or nurse giving you the infusion.

Warnings and precautions
Talk to your doctor or nurse before you are given Tyenne.

- If you experience **allergic reactions** such as chest tightness, wheezing, severe dizziness or light-headedness, swelling of the lips or skin rash during or after the infusion, then **tell your doctor immediately.**
- If you have any kind of **infection,** short- or long-term, or if you often get infections. **Tell your doctor immediately** if you feel unwell. Tyenne can reduce your body's ability to respond to infections and may make an existing infection worse or increase the chance of getting a new infection.
- If you have had **tuberculosis,** tell your doctor. Your doctor will check for signs and symptoms of tuberculosis before starting Tyenne. If symptoms of tuberculosis (persistent cough, weight loss, listlessness, mild fever), or any other infection appear during or after therapy tell your doctor immediately.
- If you have had **intestinal ulcers or diverticulitis,** tell your doctor. Symptoms would include abdominal pain and unexplained changes in bowel habits with a fever.
- If you have **liver disease,** tell your doctor. Before you use Tyenne, your doctor may do a blood test to measure your liver function.
- **If any patient has recently been vaccinated** (either adult or child), or is planning a vaccination, tell your doctor. All patients, especially children, should be up-to-date with all their vaccinations before they start treatment with Tyenne, unless urgent treatment initiation is required Certain types of vaccines should not be used while receiving Tyenne.
- If you have **cancer,** tell your doctor. Your doctor will have to decide if you can still be given Tyenne.
- If you have **risk factors for heart disease** such as raised blood pressure and raised cholesterol levels, tell your doctor. These factors need to be monitored while receiving Tyenne.
- If you have moderate to severe **kidney function problems,** your doctor will monitor you.
- If you have **persistent headaches.**

Your doctor will perform blood tests before you are given Tyenne, and during your treatment, to determine if you have a low white blood cell count, low platelet count or high liver enzymes.

Children and adolescents

Tyenne is not recommended for use in children under 2 years of age.

If a child has a history of **macrophage activation syndrome,** (activation and uncontrolled proliferation of specific blood cells), tell your doctor. Your doctor will have to decide if they can still be given Tyenne.

Other medicines and Tyenne
Tell your doctor if you are taking any other medicines (or your child is, if they are the patient), or have recently taken any. This includes medicines obtained without a prescription. Tyenne 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 (such as amlodipine), used to treat high 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 (such as temazepam), used to relieve anxiety.

Regarding vaccinations, please see the section on warnings above.

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

Pregnancy and breast-feeding
Tyenne is not to be used in pregnancy unless clearly necessary. Talk to your doctor if you are pregnant, may be pregnant, or intend to become pregnant.

Women of childbearing potential must use effective contraception during and up to 3 months after treatment.

Stop breast-feeding if you are to be given Tyenne, and talk to your doctor. Leave a gap of at least 3 months after your last treatment before you start breast-feeding. It is not known whether Tyenne passes into breast milk.

The data available so far does not suggest any effect on fertility from this treatment.

Driving and using machines
This medicine can cause dizziness. If you feel dizzy, do not drive or use machines.

Tyenne contains sodium
This medicine contains 34.8 mg sodium per maximum dose of 1200 mg. Take this into account if you are on a low-sodium diet. However, doses below 800 mg of this medicine contain less than 23 mg sodium, so they are essentially sodium free.

3. How Tyenne is given

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

Tyenne will be given to **you as a drip into a vein, by a doctor or a nurse.** They will dilute the solution, set up the intravenous infusion and monitor you during and after the treatment.

Adult patients with RA
The usual dose of Tyenne is 8 mg per kg of body weight. Depending on your response, your doctor may decrease your dose to 4 mg/kg then increase back to 8 mg/kg when appropriate.

Adults will be given Tyenne once every 4 weeks through a drip in the vein (intravenous infusion) over one hour.

Children with sJIA (aged 2 and over)
The usual dose of Tyenne depends on your weight.
- If you weigh less than 30 kg: the dose is 12 mg for every kilogram of body weight
- If you weigh 30 kg or more: the dose is 8 mg for every kilogram of body weight

The dose is calculated based on your body weight at each administration.

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

Children with pJIA (aged 2 and over)
The usual dose of Tyenne depends on your weight.
- If you weigh less than 30 kg: the dose is 10 mg for every kilogram of body weight
- If you weigh 30 kg or more: the dose is 8 mg for every kilogram of body weight

The dose is calculated based on your body weight at each administration.

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

Patients with CRS
The usual dose of Tyenne is 8 mg for every kg of body weight if you weigh 30 kg or more.
The dose is 12 mg for every kg of body weight if you weigh less than 30 kg.
Tyenne can be given alone or in combination with corticosteroids.

Patients with COVID-19
The usual dose of Tyenne is 8 mg for every kg of body weight. A second dose may be required.

If you are given more Tyenne than you should
Since Tyenne is given by a doctor or nurse, it is unlikely that you will be given too much.
However, if you are worried, talk to your doctor.

If you miss a dose of Tyenne
Since Tyenne 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 receiving Tyenne
You should not stop receiving Tyenne without discussing with your doctor first.

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

4. Possible side effects

Like all medicines, Tyenne can cause side effects, although not everybody gets them. Side effects could occur at least up to 3 months after your last dose of Tyenne.

Possible serious side effects: tell a doctor straight away.
These are common: they may affect up to 1 in 10 people

Allergic reactions during or after infusion:
- difficulty with breathing, chest tightness or light-headedness
- rash, itching, hives, swelling of the lips, tongue or face

If you notice any of these, tell your doctor **immediately**.

Signs of serious infections
- fever and chills
- mouth or skin blisters
- stomach ache

Signs and symptoms of liver toxicity
These may affect up to 1 in 1000 people
- tiredness,
- abdominal pain,
- jaundice (yellow discolouration of skin or eyes)

If you notice any of these, tell your doctor **as soon as possible.**

Very common side effects:
These 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:
These may affect up to 1 in 10 people
- lung infection (pneumonia)
- shingles (herpes zoster)
- cold sores (oral herpes simplex), blisters
- skin infection (cellulitis) sometimes with fever and chills
- rash and itching, hives
- allergic (hypersensitivity) reactions
- eye infection (conjunctivitis)
- headache, dizziness, high blood pressure
- mouth ulcers, stomach pain
- fluid retention (oedema) in the lower legs, weight increase
- cough, shortness of breath
- low white blood cell counts shown by blood tests (neutropenia, leucopenia)
- abnormal liver function tests (increased transaminases)
- increased bilirubin shown by blood tests
- low fibrinogen levels in the blood (a protein involved in blood clotting).

Uncommon side effects:
These may affect up to 1 in 100 people
- diverticulitis (fever, nausea, diarrhoea, constipation, stomach pain)
- red swollen areas in the mouth
- high blood fat (triglycerides)
- stomach ulcer
- kidney stones
- underactive thyroid.

Rare side effects:
These may affect up to 1 in 1000 people
- Stevens-Johnson syndrome (skin rash, which may lead to severe blistering and peeling of the skin)
- fatal allergic reactions (anaphylaxis [fatal])
- inflammation of the liver (hepatitis), jaundice

Very rare side effects:
These may affect up to 1 in 10000 people
- low counts for white blood cells, red blood cells and platelets in blood tests
- liver failure

Children with sJIA
In general, side effects in sJIA patients were of a similar type to those in adults with RA. Some side effects were seen more often: inflamed nose and throat, diarrhoea, lower white blood cell counts and higher liver enzymes.

Children with pJIA
In general, side effects in pJIA patients were of a similar type to those in adults with RA. Some side effects were seen more often: inflamed nose and throat, headache, feeling sick (nausea) and lower white blood cell counts.

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.

Ireland
HPRA Pharmacovigilance
Website: www.hpra.ie

UK
Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

5. How to store Tyenne

Keep Tyenne out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the carton.
Store in a refrigerator (2°C - 8°C). Do not freeze.
Keep the vial in the outer carton in order to protect from light.

6. Contents of the pack and other information

What Tyenne contains
- The active substance is tocilizumab.
  Each 4 mL vial contains 80 mg tocilizumab (20 mg/mL).
  Each 10 mL vial contains 200 mg tocilizumab (20 mg/mL).
  Each 20 mL vial contains 400 mg tocilizumab (20 mg/mL).
- The other ingredients are L-arginine, L-histidine, L-lactic acid, sodium chloride, polysorbate 80, hydrochloric acid (E507) and/or sodium hydroxide (E524), water for injections.

Regarding sodium, please see section 2 "Tyenne contains sodium" above.

What Tyenne looks like and contents of the pack
Tyenne is a concentrate for solution for infusion. The concentrate is a clear and colourless to pale yellow liquid. Tyenne is supplied as vials containing 4 mL, 10 mL and 20 mL concentrate for solution for infusion. Each pack contains 1 vial and multipacks contain 4 (4 packs of 1) vials. Not all pack sizes may be marketed.

Marketing Authorisation Holder
For EU:
Fresenius Kabi Deutschland GmbH
Else-Kroener-Strasse 1
61352 Bad Homburg v.d.Hoehe
Germany

For GB:
Fresenius Kabi Limited
Cestrian Court
Eastgate Way, Manor Park
Runcorn, Cheshire, WA7 1NT
United Kingdom

Manufacturer
Fresenius Kabi Austria GmbH
Hafnerstrasse 36 8055 Graz Austria

This leaflet was last revised July 2023.

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu/.

The following information is intended for healthcare professionals only:

Instructions for dilution prior to administration
Parenteral medicinal products should be inspected visually for particulate matter or discolouration prior to administration. Only solutions which are clear and colourless to pale yellow and free of visible particles should be diluted. Use a sterile needle and syringe to prepare Tyenne.

RA, COVID-19 and CRS adult patients (≥ 30 kg)
Withdraw a volume of sterile, non-pyrogenic sodium chloride 9 mg/mL (0.9%) or 4.5 mg/mL (0.45%) solution for injection from a 100 mL infusion bag, equal to the volume of Tyenne concentrate required for the patients dose, under aseptic conditions. The required amount of Tyenne concentrate (0.4 mL/kg) 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.

Use in the paediatric population

sJIA, pJIA and CRS patients ≥ 30 kg
Withdraw a volume of sterile, non-pyrogenic sodium chloride 9 mg/mL (0.9%) or 4.5 mg/mL (0.45%) solution for injection from a 100 mL infusion bag, equal to the volume of Tyenne concentrate required for the patients dose, under aseptic conditions. The required amount of Tyenne concentrate (0.4 mL/kg) 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.

sJIA and CRS patients < 30 kg
Withdraw a volume of sterile, non-pyrogenic sodium chloride 9 mg/mL (0.9%) or 4.5 mg/mL (0.45%) solution for injection from a 50 mL infusion bag, equal to the volume of Tyenne concentrate required for the patients dose, under aseptic conditions. The required amount of Tyenne concentrate (0.6 mL/kg) should be withdrawn from the vial and placed in the 50 mL infusion bag. This should be a final volume of 50 mL. To mix the solution, gently invert the infusion bag to avoid foaming.

pJIA patients < 30 kg
Withdraw a volume of sterile, non-pyrogenic sodium chloride 9 mg/mL (0.9%) or 4.5 mg/mL (0.45%) solution for injection from a 50 mL infusion bag, equal to the volume of Tyenne concentrate required for the patients dose, under aseptic conditions. The required amount of Tyenne concentrate (0.5 mL/kg) should be withdrawn from the vial and placed in the 50 mL infusion bag. This should be a final volume of 50 mL. To mix the solution, gently invert the infusion bag to avoid foaming.

Tyenne is for single-use only.

Any unused product or waste material should be disposed of in accordance with local requirements.

Tyenne® 20 mg/mL
Sterile concentrate
tocilizumab

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tocilizumab

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