

Tyenne Tocilizumab

Dosing Guide

Important Safety Information for Patients

A guide to assist healthcare professionals with the dose preparation and administration of Tyenne therapy in patients with:

- Rheumatoid Arthritis
[intravenous or subcutaneous]
- Polyarticular Juvenile Idiopathic Arthritis
(also referred to as Juvenile Idiopathic Polyarthritis) [Intravenous or subcutaneous]
- Systemic Juvenile Idiopathic Arthritis
[Intravenous or subcutaneous]

This Tyenne Dosing Guide contains important safety information that you need to be aware of when administering Tyenne. This Tyenne Dosing Guide must be read together with the Tyenne Healthcare Professional and Patient Brochures and the Tyenne Labeling/Summary of Product Characteristics that comes with Tyenne, as it contains important information about Tyenne.

Please read this information carefully before administering the product.

Contents

Indications and Usage	3
-----------------------	---

Part I

Intravenous (IV) Administration of Tyenne by Infusion	5
---	---

Part II

Dosing Administration Guide With Tyenne (SC) Using Either the Pre-filled Syringe or Pre-filled Pen	10
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Indications and Usage

Tyenne IV

(Tyenne 20 mg/mL concentrate for solution for infusion)

Tyenne, in combination with methotrexate (MTX), is indicated for:

- The treatment of severe, active and progressive rheumatoid arthritis (RA) in adults not previously treated with MTX
- The treatment of moderate to severe active RA in adult patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease-modifying antirheumatic drugs (DMARDs) or tumour necrosis factor (TNF) antagonists
- In these patients, Tyenne can be given as monotherapy in case of intolerance to MTX, or where continued treatment with MTX is inappropriate.
- Tyenne has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function when given in combination with methotrexate.
- Tyenne is indicated for the treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 2 years of age and older, who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids.
- In these patients, Tyenne can be given as monotherapy (in case of intolerance to MTX or where treatment with MTX is inappropriate), or in combination with MTX.
- Tyenne in combination with methotrexate (MTX) is indicated for the treatment of juvenile idiopathic polyarthritis (pJIA; rheumatoid factor positive or negative) in patients 2 years of age and older, who have responded inadequately to previous therapy with MTX.
- In these patients, Tyenne can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.

Tyenne SC

(Tyenne 162 mg solution for injection in pre-filled syringe)

In combination with methotrexate (MTX), Tyenne is indicated for:

- The treatment of severe, active and progressive rheumatoid arthritis (RA) in adults not previously treated with MTX
- The treatment of moderate to severe active RA in adult patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease-modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) antagonists
- In these patients, Tyenne can be given as monotherapy in case of intolerance to MTX, or where continued treatment with MTX is inappropriate.
- Tyenne has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function when given in combination with methotrexate.
- Tyenne is indicated for the treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 2 year of age and older, who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids.
- In these patients, Tyenne can be given as monotherapy (in case of intolerance to MTX or where treatment with MTX is inappropriate), or in combination with MTX.
- Tyenne in combination with methotrexate (MTX) is indicated for the treatment of juvenile idiopathic polyarthritis (pJIA; rheumatoid factor positive or negative) in patients 2 years of age and older, who have responded inadequately to previous therapy with MTX.
- In these patients, Tyenne can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.

Tyenne SC

(Tyenne 162 mg solution for injection in pre-filled pen)

Tyenne, in combination with methotrexate (MTX), is indicated for:

- The treatment of severe, active and progressive rheumatoid arthritis (RA) in adults not previously treated with MTX
- The treatment of moderate to severe active RA in adult patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease-modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) antagonists
- In these patients, Tyenne can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.
- Tyenne is indicated for the treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 12 years of age and older, who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids.
- Tyenne can be given as monotherapy (in case of intolerance to MTX, or where treatment with MTX is inappropriate) or in combination with MTX.
- Tyenne in combination with methotrexate (MTX) is indicated for the treatment of juvenile idiopathic polyarthritis (pJIA; rheumatoid factor positive or negative) and extended oligoarthritis in patients 12 years of age and older, who have responded inadequately to previous therapy with MTX.
- Tyenne can be given as monotherapy in case of intolerance to MTX, or where continued treatment with MTX is inappropriate.

Tyenne SC formulation is administered with a single-use pre-filled pen. Treatment should be initiated by healthcare professionals experienced in the diagnosis and treatment of RA, sJIA, pJIA.

The pre-filled pen should not be used to treat paediatric patients < 12 years of age since there is a potential risk of intramuscular injection due to thinner subcutaneous tissue layer.

The first injection should be performed under the supervision of a qualified healthcare professional. A patient or parent/guardian can inject Tyenne only if the physician determines that it is appropriate and the patient or parent/guardian agrees to medical follow-up as necessary and has been trained in proper injection technique.

Patients who transition from Tyenne IV therapy to SC administration should administer the first SC dose at the time of the next scheduled IV dose under the supervision of a qualified health care professional.

All patients treated with Tyenne should be given the Patient Alert Card.

Suitability of the patient or parent/guardian for subcutaneous home use should be assessed and patients or their parent/guardian should be instructed to inform a healthcare professional before administering the next dose if they experience symptoms of an allergic reaction.

Patients should seek immediate medical attention if developing symptoms of serious allergic reactions.

Prior to starting treatment with Tyenne:

- It is important that you review the pre-administration checklist found in the Patient Brochure: **Tyenne (Tocilizumab) Patient Brochure, Important Safety Information for Patients** with your patient, the patient's parents/guardians, or both.
- Allow ample time to discuss any questions your patient, the patient's parents/guardians, or both may have.
- It is important that you review the information contained within the Healthcare Professional Brochure for Tyenne (tocilizumab) intravenous (IV) and subcutaneous (SC) formulations and the Patient Brochure: **Before starting treatment with Tyenne (tocilizumab)** with your patient, the patient's parents/guardians, or both. These will help them understand what they may expect from the treatment of the patient's condition with Tyenne.

For full information, see the Summary of Product Characteristics (SmPC) and the Tyenne Package Leaflet.

Tyenne Patient Brochures and other information can be requested from your sales representative.

Part I

Intravenous (IV) Administration of Tyenne by Infusion

This guide will walk you through the Tyenne infusion process in 6 steps.

STEP 1:

Weigh Patient and Calculate Tyenne Dose Based on Indication

Tyenne dosing is calculated based on each patient's weight and the indication for which they are treated. The treatment frequency varies by indication. Verify the patient's weight and indication, then locate it on the chart to find the corresponding dose and recommended vial combination.

If the patient's dose has been calculated prior to the infusion date, take his or her weight to make sure that it has not changed from the time of the original calculation to require a change in dose. If the patient's weight has changed, contact the prescriber to discuss whether a dosing change is needed. Refer to the chart to check whether a dosing adjustment is necessary.

Once the dose is calculated, choose the vial combination of Tyenne that best matches the patient's needs. Tyenne is available in three different dosing vials:



Inspect the vials for particulate matter and discoloration. Only solutions which are clear to opalescent, colourless to pale yellow and free of visible particles should be used.

8 mg/kg dose				
Weight (kg)	Weight (lbs)	Dose (mg)	Dose (mL)	Vial Combinations
50	110.0	400	20.0	
52	114.4	416	20.8	+
54	118.8	432	21.6	+
56	123.2	448	22.4	+
58	127.6	464	23.2	+
60	132.0	480	24.0	+
62	136.4	496	24.8	+ + +
64	140.8	512	25.6	+ + +
66	145.2	528	26.4	+
68	149.6	544	27.2	+
70	154.0	560	28.0	+
72	158.4	576	28.8	+
74	162.8	592	29.6	+
76	167.2	608	30.4	+ +
78	171.6	624	31.2	+ +
80	176.0	640	32.0	+ +
82	180.4	656	32.8	+
84	184.8	672	33.6	+
86	189.2	688	34.4	+ + +
88	193.6	704	35.2	+ + +
90	198.0	720	36.0	+ + +
92	202.4	736	36.8	+ +
94	206.8	752	37.6	+ +
96	211.2	768	38.4	+
98	215.6	784	39.2	+
≥100	≥220.0	800	40.0	+

RA: Dosing Preparation and Administration Guide with Tyenne IV

Dosing should take place at 4-week intervals.

Tyenne IV dosing in RA patients is calculated based on each patient's weight as follows:

For the 8 mg/kg dose:
Patient weight (kg) × 8 (mg/kg) = Tyenne ___ mg dose

For individuals whose body weight is more than 100 kg, doses exceeding 800 mg per infusion are not recommended.

pJIA: Dosing Preparation and Administration Guide with Tyenne IV

Dosing should take place at 4-week intervals.

A change in dose of 8mg/kg or 10 mg/kg should only be based on a consistent change in the patient's body weight over time (e.g., within 3 weeks). If the patient's weight has changed, contact the prescriber to discuss whether a dosing change is needed. Refer to the chart to check whether a dosing adjustment is necessary.

Tyenne IV dosing in pJIA patients is calculated based on each patient's weight as follows:

For patients weighing <30 kg:

Patient weight (kg) × 10 (mg/kg) = Tyenne dose

For patients weighing ≥30 kg:

Patient weight (kg) × 8 (mg/kg) = Tyenne dose

10 mg/kg dose				
Weight (kg)	Weight (lbs)	Dose (mg)	Dose (mL)	Vial Combinations
10	22.0	100	5.0	
12	26.4	120	6.0	
14	30.8	140	7.0	
16	35.2	160	8.0	
18	39.6	180	9.0	
20	44.0	200	10.0	
22	48.4	220	11.0	
24	52.8	240	12.0	
26	57.2	260	13.0	
28	61.6	280	14.0	

8 mg/kg dose				
Weight (kg)	Weight (lbs)	Dose (mg)	Dose (mL)	Vial Combinations
30	66.0	240	12.0	
32	70.4	256	12.8	
34	74.8	272	13.6	
36	79.2	288	14.4	
38	83.6	304	15.2	
40	88.0	320	16.0	
42	92.4	336	16.8	
44	96.8	352	17.6	
46	101.2	368	18.4	
48	105.6	384	19.2	
50	110.0	400	20.0	
52	114.4	416	20.8	
54	118.8	432	21.6	
56	123.2	448	22.4	
58	127.6	464	23.2	
60	132.0	480	24.0	
62	136.4	496	24.8	
64	140.8	512	25.6	
66	145.2	528	26.4	
68	149.6	544	27.2	
70	154.0	560	28.0	
72	158.4	576	28.8	
74	162.8	592	29.6	
76	167.2	608	30.4	
78	171.6	624	31.2	
80	176.0	640	32.0	
82	180.4	656	32.8	
84	184.8	672	33.6	
86	189.2	688	34.4	
88	193.6	704	35.2	
90	198.0	720	36.0	
92	202.4	736	36.8	
94	206.8	752	37.6	
96	211.2	768	38.4	
98	215.6	784	39.2	
≥100	≥220.0	800	40.0	

sJIA: Dosing Preparation and Administration Guide with Tyenne IV

Dosing should take place at 2-week intervals.

A change in dose of 8mg/kg or 12 mg/kg should only be based on a consistent change in the patient's body weight over time (e.g., within 3 weeks). If the patient's weight has changed, contact the prescriber to discuss whether a dosing change is needed. Refer to the chart to check whether a dosing adjustment is necessary.

Tyenne dosing in sJIA patients is calculated based on each patient's weight as follows:

For patients weighing <30 kg:

Patient weight (kg) × 12 (mg/kg) = Tyenne dose

For patients weighing ≥30 kg:

Patient weight (kg) × 8 (mg/kg) = Tyenne dose

12 mg/kg dose				
Weight (kg)	Weight (lbs)	Dose (mg)	Dose (mL)	Vial Combinations
10	22.0	120	6.0	
12	26.4	144	7.2	
14	30.8	168	8.4	
16	35.2	192	9.6	
18	39.6	216	10.8	
20	44.0	240	12.0	
22	48.4	264	13.2	
24	52.8	288	14.4	
26	57.2	312	15.6	
28	61.6	336	16.8	

8 mg/kg dose				
Weight (kg)	Weight (lbs)	Dose (mg)	Dose (mL)	Vial Combinations
30	66.0	240	12.0	
32	70.4	256	12.8	
34	74.8	272	13.6	
36	79.2	288	14.4	
38	83.6	304	15.2	
40	88.0	320	16.0	
42	92.4	336	16.8	
44	96.8	352	17.6	
46	101.2	368	18.4	
48	105.6	384	19.2	
50	110.0	400	20.0	
52	114.4	416	20.8	
54	118.8	432	21.6	
56	123.2	448	22.4	
58	127.6	464	23.2	
60	132.0	480	24.0	
62	136.4	496	24.8	
64	140.8	512	25.6	
66	145.2	528	26.4	
68	149.6	544	27.2	
70	154.0	560	28.0	
72	158.4	576	28.8	
74	162.8	592	29.6	
76	167.2	608	30.4	
78	171.6	624	31.2	
80	176.0	640	32.0	
82	180.4	656	32.8	
84	184.8	672	33.6	
86	189.2	688	34.4	
88	193.6	704	35.2	
90	198.0	720	36.0	
92	202.4	736	36.8	
94	206.8	752	37.6	
96	211.2	768	38.4	
98	215.6	784	39.2	
≥100	≥220.0	800	40.0	

STEP 2:

Gather All Necessary Supplies

You will need:

- Tyenne, at room temperature
- Syringes and large-bore needles
- One primary infusion set
- One 100 mL or 50 mL (for patients <30kg) bag of 0.9% (9 mg/mL) sterile, non-pyrogenic sodium chloride solution for injection
- Gauze
- Tourniquet
- Gloves
- Alcohol/cleansing wipes
- One intravenous (IV) catheter

STEP 3:

Take Baseline Assessments

Take baseline assessments to ensure the patient is healthy enough to receive the infusion.

Vital signs may include:

- Blood pressure
- Temperature
- Pulse

Follow the recommended baseline patient questions as described in the Tyenne Healthcare Provider Brochure (Section 15 – General Recommendation) as well as the Summary of Product Characteristics (Section 4.4 – Warnings and Precautions).

STEP 4:

Prepare the Patient for the Infusion

Review the Patient Brochure with the patient before starting treatment with Tyenne® (tocilizumab). Answer any questions he or she might have.

Tyenne does not require premedication.

STEP 5:

Prepare the Tyenne Infusion

Tyenne is a ready-mix solution and requires no reconstitution.

The expiry date should always be checked before use.

The Tyenne concentrate for IV infusion should be diluted by a healthcare professional using aseptic technique.

- Tyenne should be refrigerated for storage. However, the fully diluted Tyenne solution should be allowed to reach room temperature before it is infused.
- The fully diluted Tyenne solutions for infusion may be stored at 2°C–8°C or room temperature (if diluted under controlled and validated aseptic conditions) for up to 24 hours and should be protected from light.
- Tyenne solutions do not contain preservatives; therefore, unused product remaining in the vials should not be used.
- **Weight-/indication-based dosing:**
 - For RA, sJIA (>30 kg), and pJIA (>30 kg): From a 100 mL infusion bag, withdraw a volume of 0.9% (9 mg/mL) sterile, non-pyrogenic sodium chloride solution for injection equal to the volume of the Tyenne solution required for the patient's dose.
 - For sJIA and pJIA patients < 30 kg: From a 50 mL infusion bag, withdraw a volume of 0.9% (9 mg/mL) sterile, non-pyrogenic sodium chloride solution for injection equal to the volume of the Tyenne solution required for the patient's dose.
- Tyenne should not be infused concomitantly in the same IV line with other medications. No physical or biochemical compatibility studies have been conducted to evaluate the co-administration of Tyenne with other medications.
- Slowly add Tyenne concentrate for IV infusion from each vial into the infusion bag. To mix the solution, gently invert the bag to avoid foaming.
- Parenteral medicinal products should be inspected visually for particulate matter and discoloration prior to administration. Only solutions which are clear to opalescent, colourless to pale yellow and free of visible particles should be diluted.
- Dispose of needle and syringe in sharps containers when finished.

STEP 6:

Begin the Tyenne Infusion

The infusion should be administered over 60 minutes.

It must be administered with an infusion set and should never be administered as an IV push or bolus.

- Prior to the infusion, inform the patient that serious allergic reactions including anaphylaxis have been reported in association with Tyenne. Such reactions may be more severe, and potentially fatal, in patients who have experienced allergic reactions during previous treatment with Tyenne, even if they have received premedication with steroids and antihistamines. Most allergic reactions occur during infusion or within 24 hours of Tyenne administration, although allergic reactions can occur at any time.
- If an anaphylactic reaction or other serious hypersensitivity reaction occurs, administration of Tyenne should be stopped immediately, appropriate therapy initiated and Tyenne should be permanently discontinued. Fatal anaphylaxis has been reported after marketing authorisation during treatment with IV Tyenne.
- Instruct the patient to seek immediate medical attention if they notice any of the following signs or symptoms of systemic allergic reactions after receiving Tyenne:
 - Rash, itching or hives
 - Shortness of breath or trouble breathing
 - Swelling of the lips, tongue or face
 - Chest pain
 - Feeling dizzy or faint
 - Severe stomach pain or vomiting
 - Hypotension

Once the infusion is completed, remove the catheter and dispose of all supplies properly, bandage the infusion site and check the patient's vital signs

Part II

Dosing Administration Guide with Tyenne SC, Using Either the Pre-filled Syringe or Pre-filled Pen

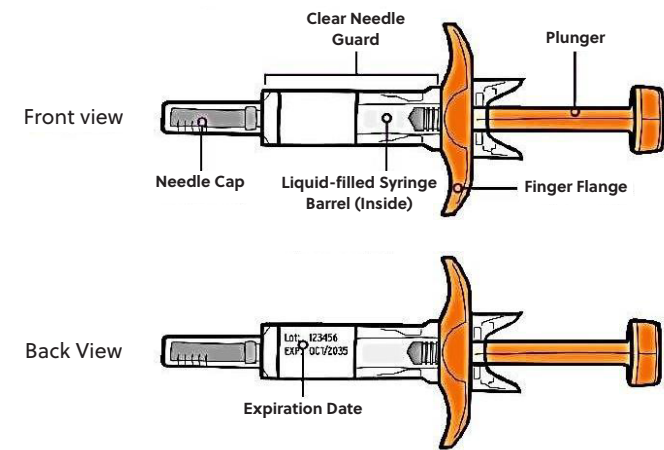
Instructions for Pre-filled Syringe

The pre-filled syringe is used in the RA, pJIA, and sJIA indications only.

This guide will walk you through the Tyenne SC injection process in 8 steps.

Tyenne Pre-filled Syringe

Before Use



After Use

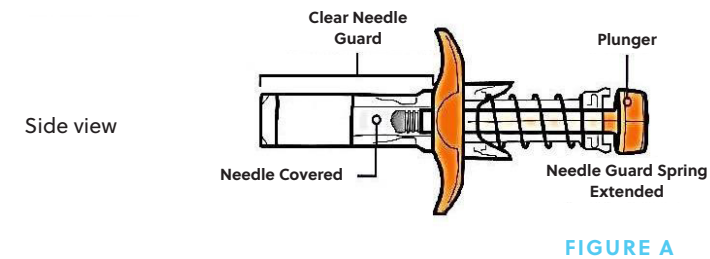


FIGURE A

! Do not try to activate the clear needle guard before injecting.

STEP 1:

Prepare for Your Injection

1.1: Prepare a clean, flat surface, such as a table or counter top, in a well-lit area.

1.2: Supplies Needed (Figure B):

- 1 alcohol swab to clean the site before injection
- 1 sterile cotton ball or gauze to use after the injection
- 1 sharps disposal container for safe disposal of needle cap and used syringe (see Step 7 "Throw away your syringe").



FIGURE B

1.3: Take the Tyenne carton out of the refrigerator and open it (Figure C).

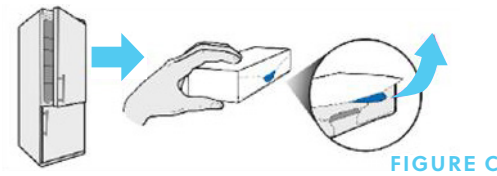


FIGURE C

1.4: Remove Tyenne sealed plastic tray from the carton:

- Put the sealed plastic tray with the pre-filled syringe on a clean flat surface.

1.5: Let the pre-filled syringe in its sealed plastic tray sit at room temperature for at least 30 minutes before use to allow the medicine to reach room temperature (Figure D). Injecting cold medicine can cause your injection to feel uncomfortable and make it difficult to push the plunger in.



FIGURE D

! Do not speed up the warming process in any way, such as in a microwave, or placing the syringe in hot water, or direct sunlight.

! Do not remove the needle cap while allowing your Tyenne pre-filled syringe to reach room temperature.

1.6: Prepare and check your records of previous injection sites. This will help you choose the appropriate injection site for this injection (see Step 8 "Record your injection").

STEP 2:

Wash Your Hands

2.1: Wash your hands well with soap and water and dry them with a clean towel (Figure E).



FIGURE E

STEP 3:

Check the Syringe

Remove Tyenne pre-filled syringe from the sealed plastic tray

- Peel off the seal from the sealed plastic tray.
- Place two fingers on either side, in the middle of the clear needle guard.
- Pull the pre-filled syringe straight up and out of the tray (Figure F).

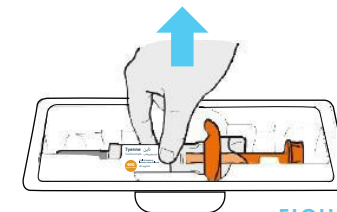


FIGURE F

! Do not pick up the pre-filled syringe by the plunger or the needle cap. Doing so could damage the pre-filled syringe or activate the clear needle guard.

3.1: Check the pre-filled syringe to make sure that:

- The pre-filled syringe, the clear needle guard, and the needle cap are not cracked or damaged (Figure G).
- The needle cap is securely attached (Figure H).
- The needle guard spring is not extended (Figure I)

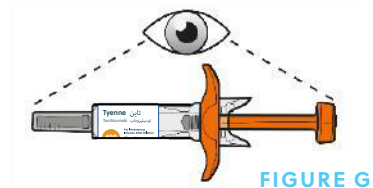


FIGURE G

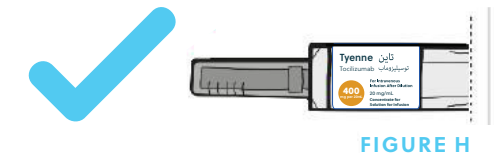


FIGURE H

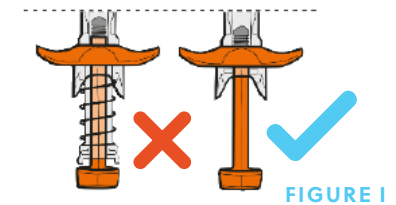


FIGURE I

! Do not use the syringe if it shows any sign of damage. If damaged, call your doctor or pharmacist right away and throw away the syringe in your sharps disposal container (see Step 7 "Throw away your syringe").

3.2: Check the liquid through the clear window of the syringe to make sure that:

- The liquid is clear and colorless to pale yellow, and free of particles and flakes (Figure J).



FIGURE J

⚠ Do not use the pre-filled syringe if the liquid is cloudy, discolored, contains particles or flakes, or shows any sign of damage. If the liquid is cloudy, discolored, or contains particles or flakes, call your doctor or pharmacist right away and throw away the syringe in your sharps disposal container (see Step 7 "Throw away your syringe")

3.3: Check the label on the pre-filled syringe to make sure that:

- The name on the pre-filled syringe says Tyenne (Figure K).
- The expiration date (EXP:) on the pre-filled syringe has not passed (Figure K).

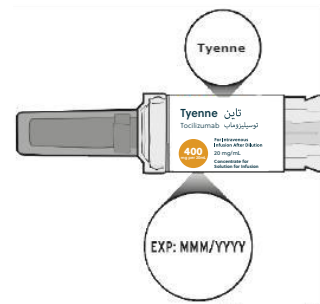


FIGURE K

⚠ Do not use the pre-filled syringe if:

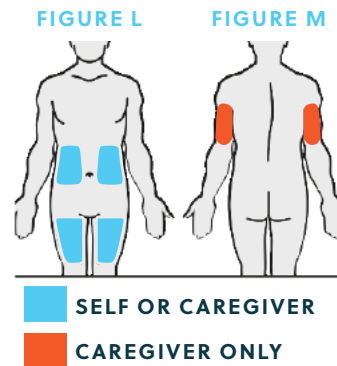
- The name on the pre-filled syringe is not Tyenne.
- The expiration date on the pre-filled syringe has passed.

If the label does not have Tyenne on it or the expiration date has passed, contact your doctor or pharmacist right away and throw away the pre-filled syringe in your sharps disposal container (see Step 7 "Throw away your syringe").

STEP 4:
Choose the Injection Site

4.1: Choose an injection site (Figure L):

- The front of the thighs, or
- Stomach area (lower abdomen), except for 5 cm around the navel (belly button).
- If you are injecting someone else, you may use the back of the arm (Figure M).



⚠ Do not attempt to use the upper arm area by yourself. Only inject into the sites shown.

4.2: Choose a different injection site (at least 3 cm from the last area you injected) for each new injection to reduce redness, irritation or other skin problems.

⚠ Do not inject into an area that is sore (tender), bruised, red, hard, scarred or where you have stretch marks, moles or tattoos.

⚠ If you have psoriasis, do not inject into any lesions or red, thick, raised or scaly patches.

STEP 5:
Clean the Injection Site

5.1: Wipe the skin of your injection site with an alcohol swab in a circular motion to clean it (Figure N). Let the skin dry before injecting.

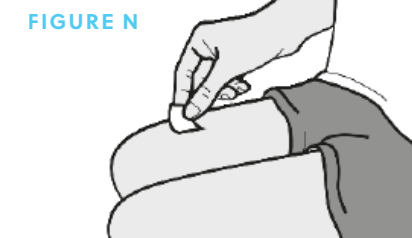


FIGURE N

STEP 6:
Give Your Injection

6.1: When you are ready to inject, remove the needle cap

- Hold the pre-filled syringe by the clear needle guard in one hand (Figure O).
- Use your other hand to remove the needle cap by pulling the cap straight off (Figure O).

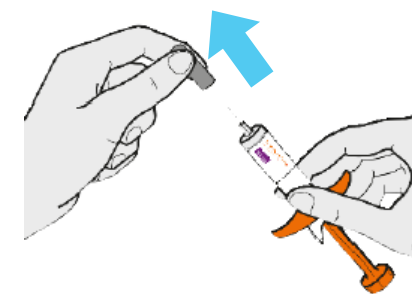


FIGURE O

⚠ Do not hold the plunger while you remove the needle cap. Note: after removing the cap, use the pre-filled syringe right away to prevent the medicine from drying out and blocking the needle.

⚠ Do not try to recap the needle at any time, even at the end of the injection.

⚠ If you cannot remove the needle cap, you should ask a caregiver for help or contact your doctor.

- Throw away the needle cap in your sharps container.

⚠ You may see drops of liquid at the needle tip. This is normal and will not affect your dose.

⚠ Do not touch the needle or let it touch any surface after removing the needle cap, because this might cause an accidental needle stick.

6.2: Pinch the skin

- With your free hand, gently pinch around the area where you plan to inject (without squeezing or touching the cleaned area) and hold it firmly to avoid injecting into muscle (Figure P). Injection into muscle could cause the injection to feel uncomfortable.



FIGURE P

6.3: Insert the needle

Hold the pre-filled syringe like a pencil.

- With a quick, short motion, insert the needle all the way into the pinched skin at an angle between 45° to 90° (Figure Q). Give the injection at the angle your doctor instructed you to use. It is important to use the correct angle to make sure the medicine is delivered under the skin (into fatty tissue), or the injection could be painful, and the medicine may not work.

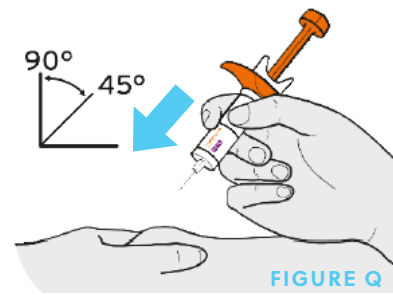


FIGURE Q

6.4: Inject

- Use your thumb to gently push the plunger all the way down (Figure R).
- Keep pressing down on the plunger to deliver the full dose until you cannot press any more (Figure S).

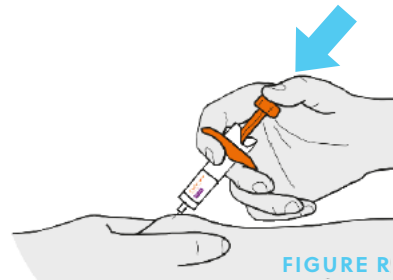


FIGURE R

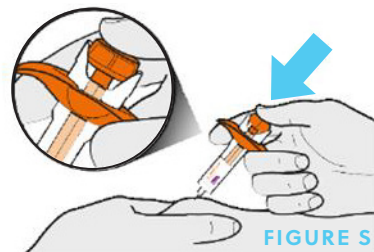


FIGURE S

! Do not pull the needle out of the skin when the plunger is pushed all the way down.

6.5: Finish Injection

- Hold the syringe firmly without moving it, at the same angle as inserted.
- Slowly release your thumb off the plunger. The plunger will move up.
- The safety system will remove the needle from the skin and cover the needle (Figure T).
- Release the pinched skin

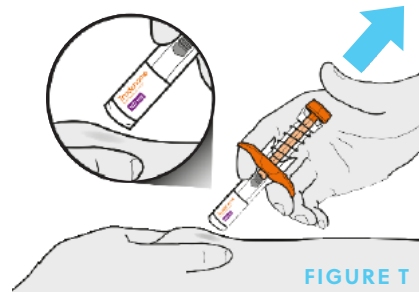


FIGURE T

! **Important:** Call your doctor right away if:

- The clear needle guard does not cover the needle after injecting. Injecting an incorrect amount of medicine could affect your treatment.

! Do not reuse a syringe even if all of the medicine was not injected.

! Do not try to recap the needle as it could lead to needle stick injury.

6.6: After Injection

If there is blood or liquid on the injection site, gently press a cotton ball or gauze on the skin (Figure U). You may use an adhesive bandage if needed.



FIGURE U

! Do not rub the injection site.

! Keep Tyenne pre-filled syringes and disposal container out of the reach of children.

STEP 7:
Throw Away Used Pre-Filled Syringe

7.1: Put your used syringe in a sharps disposal container right away after use (Figure V).

If you do not have a sharps disposal container, you may use a household container that is:

- Made of a heavy-duty plastic;
- Can be closed with a tight-fitting, puncture-resistant lid; that will keep sharps from coming out,
- Upright and stable during use,
- Leak-resistant and
- Properly labeled to warn of hazardous waste inside the container

When your sharps disposal container is almost full, you will need to follow your local guidelines to dispose of your sharps disposal container.

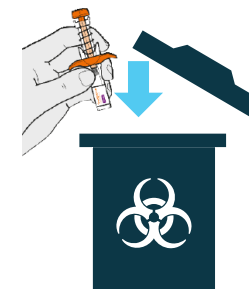


FIGURE V

! Do not throw away (dispose of) used syringes in your household trash.

! Do not dispose of your used sharps disposal container in your household trash unless your local guidelines permit this.

! Do not recycle your used sharps disposal container.

STEP 8:
Record Your Injection

8.1: To help you remember when and where to give your next injection, write the date, time, and specific part of your body where you injected yourself. (Figure W).

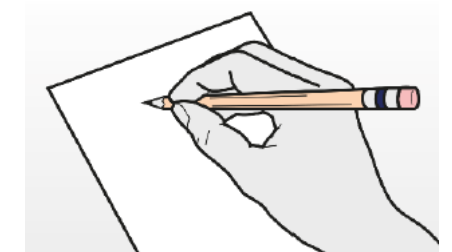


FIGURE W

If you have questions or concerns about your Tyenne pre-filled syringe, please contact your doctor familiar with Tyenne.

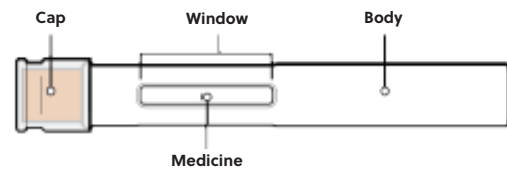
Instructions for Pre-filled Pen

The pre-filled pen is used in the RA, pJIA, and sJIA indications only.

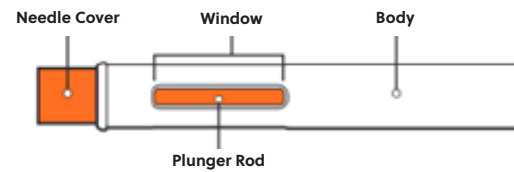
This guide will walk you through the Tyenne SC pen process in 9 steps.

Tyenne Pre-filled Pen

Before Use



After Use



STEP 1:

Prepare for Your Injection

1.1: Prepare a clean, flat surface, such as a table or counter top, in a well-lit area.

1.2: Gather the following supplies (not included) (see Figure A):

- A sterile cotton ball or gauze
- An alcohol swab
- A sharps disposal container (see Step 8, "Throw away your pre-filled pen").



FIGURE A

1.3: Remove the carton containing the pre-filled pen from the refrigerator.

⚠ Do not keep your pre-filled pen out of the refrigerator for more than 14 days without use.

1.4: Check the expiration date on the carton to make sure the date has not passed (see Figure B).



FIGURE B

⚠ Do not use the pre-filled pen if the expiration date has passed.

1.5: Remove the sealed tray from the carton. Check the sealed tray for any signs of damage, and make sure the expiration date on the tray has not passed.

⚠ Do not use the pre-filled pen if the expiration date has passed, because it may not be safe.

⚠ Do not use the pre-filled pen if the tray looks damaged or like it has been opened.

1.6: Let the sealed tray sit on the prepared surface for 45 minutes before use to allow the medicine in the pre-filled pen to reach room temperature (see Figure C).



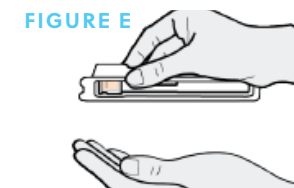
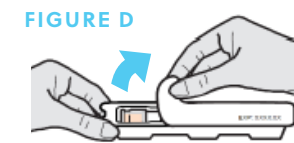
FIGURE C

⚠ **Note:** Not doing so could cause your injection to feel uncomfortable and it could take longer to inject.

⚠ Do not warm in any other way, such as in a microwave, hot water, or direct sunlight.

🚫 **Keep Tyenne out of the reach of children.**

1.7: Peel the seal off of the tray (see Figure D), and invert the tray to remove the single-use pre-filled pen (see Figure E).



⚠ Do not remove the clear cap of the pre-filled pen until you are ready to inject to avoid injury.

STEP 2:

Check Your Pre-Filled Pen

2.1: Check the pre-filled pen to make sure it is not cracked or damaged (see Figure F).

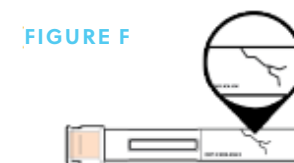


FIGURE F

⚠ Do not use if the pre-filled pen shows signs of damage, or if it has been dropped.

2.2: Check the pre-filled pen label to make sure that:

- The name on the pre-filled pen says Tyenne.
- The expiration date (EXP): on the pre-filled pen has not passed (see Figure G).

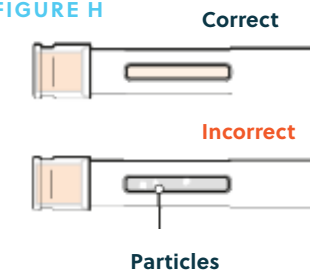
FIGURE G



⚠ Do not use the pre-filled pen if the name on the label is not Tyenne, or the expiration date on the label has passed.

2.3: Look at the medicine in the viewing window. Make sure it is clear and colorless to pale yellow and does not contain flakes or particles (see Figure H).

FIGURE H



Note: Air bubbles in the medicine are normal.

⚠ Do not inject if the liquid is cloudy, discolored, or has lumps or particles in it because it may not be safe to use.

STEP 3:
Wash Your Hands

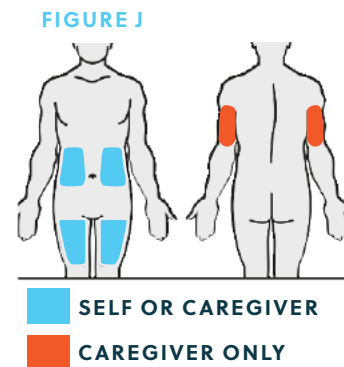
3.1: Wash your hands well with soap and water, then dry them with a clean towel (see *Figure I*).



STEP 4:
Choose the Injection Site

4.1: If you are giving yourself the injection, you can use:

- The front of your upper thigh
- The abdomen, except within 5cm around the navel (belly button)
- If a caregiver is giving the injection, they can use the outer area of the upper arm (see *Figure J*).



Note: Choose a different site for each injection to reduce redness, irritation or other skin problems.

⚠ Do not inject into skin that is sore (tender), bruised, red, hard, scaly, or has lesions, moles, scars, or stretch marks or tattoos.

⚠ Do not use the pre-filled pen through clothing.

STEP 5:
Clean the Injection Site

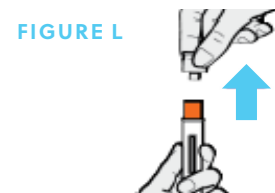
5.1: Wipe the skin where you want to inject with an alcohol swab to clean it (see *Figure K*). Let the skin dry.



⚠ Do not blow on or touch the site after cleaning.

STEP 6:
Give Your Injection

6.1: When you are ready to inject, hold the pre-filled pen in one hand with the clear cap on top, pointing straight up. Using your other hand, firmly pull the clear cap straight off without twisting (see *Figure L*).



Note: Use the pre-filled pen right away after removing the cap to avoid contamination.

⚠ Do not try to recap the needle at any time, even at the end of the injection.

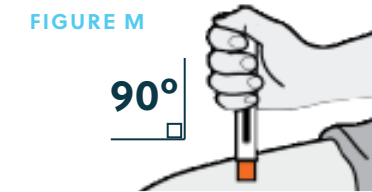
⚠ Do not touch the needle cover (the orange part located at the tip of the pre-filled pen) because this might cause an accidental needle stick.

6.2: Throw away the clear cap.

6.3: Rotate the pre-filled pen so that the orange needle cover points downwards.

6.4: Position your hand on the pre-filled pen so that you can see the window.

6.5: Place the pre-filled pen against your skin at a 90-degree (straight) angle (see *Figure M*).



Note: To make sure you inject under the skin (into fatty tissue), do not hold the pre-filled pen at an angle.

Note: You do not need to pinch your skin.

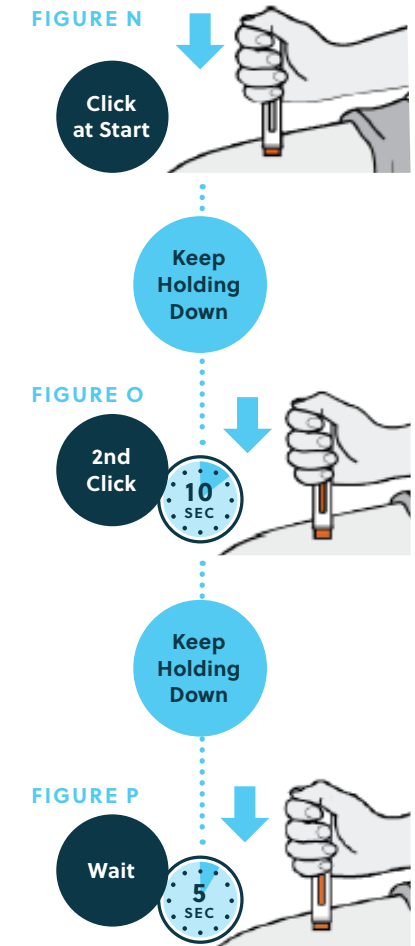
To make sure you inject the full dose, read all of the steps from 6.6 to 6.9 before you start:

6.6: In a single motion, push the pre-filled pen firmly against your skin until you hear a first click. The orange plunger rod will move through the window during the injection (this means the injection has started) (see *Figure N*).

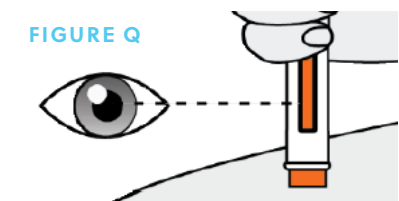
6.7: WAIT and hold the pre-filled pen in place until you hear a second click. This may take up to 10 seconds. Continue to HOLD (see *Figure O*).

6.8: Wait and slowly count to 5 after you hear the second click. Continue to HOLD the pre-filled pen in place to make sure you inject a full dose (see *Figure P*).

⚠ Do not lift the pre-filled pen until you are sure 5 seconds has passed, and the injection is complete.



6.9: While holding the pre-filled pen in place, check the window to make sure the orange plunger rod has fully appeared in the viewing window, and has stopped moving (see *Figure Q*).

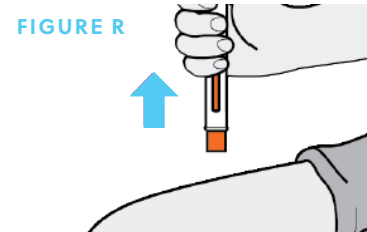


⚠ Note: If the orange plunger rod did not come all the way down, or you believe you did not get a full injection, call your doctor. Do not try to repeat the injection with a new pre-filled pen.

STEP 7:

Remove and Check the Pre-Filled Pen

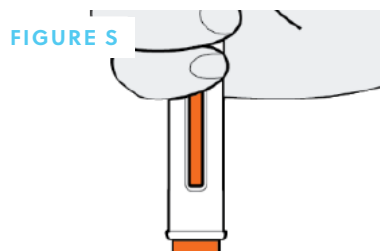
7.1: When the injection is complete, lift the pre-filled pen straight away from your skin (see *Figure R*).



Note: The needle cover will slide down and cover the needle.

Do not recap the pre-filled pen.

7.2: Check the window to make sure the orange plunger rod came all the way down (see *Figure S*).



Note: If the orange plunger rod did not come all the way down or you believe you did not get a full injection, call your doctor. Do not try to repeat the injection with a new pre-filled pen.

7.3: If you see blood on the injection site, press gauze or a cotton ball against the skin until the bleeding stops (see *Figure T*).

FIGURE T



Do not rub the injection site.

STEP 8:

Throw Away Your Pre-Filled Pen

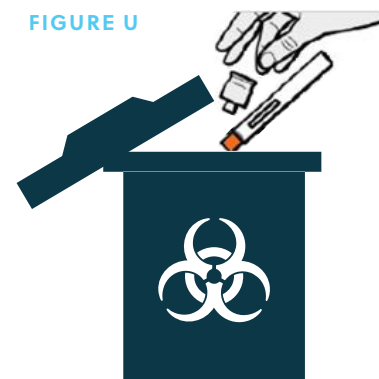
8.1: Put your used pre-filled pen in a sharps disposal container right away after use (see *Figure U*).

If you do not have a sharps disposal container, you can use a household container that is:

- made of a heavy-duty plastic,
- can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- upright and stable during use,
- leak-resistant, and
- properly labeled to warn of hazardous waste inside the container

When your sharps disposal container is almost full, you will need to follow your local guidelines for the right way to dispose of your sharps disposal container.

FIGURE U



Do not put the clear cap back on the pre-filled pen.

Do not throw away (dispose of) your pre-filled pen in your household trash.

Do not reuse the pre-filled pen.

Do not throw away (dispose of) your used sharps disposal container in your household trash unless your local guidelines permit this.

Do not recycle your used sharps disposal container.

Always keep the sharps disposal container out of reach of children.

STEP 9:

Record Your Injection

9.1: Record your injection date and site (see *Figure V*).

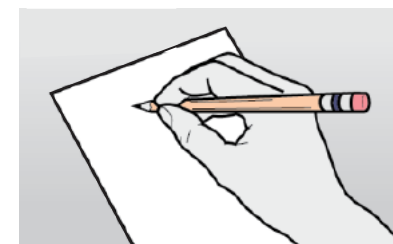


FIGURE V

Note: This is to help you remember when and where to do your next injection.

Call for Reporting

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

By reporting side effects, you can help provide more information on the safety of this medicine.

Please report any suspected adverse reactions associated with the use of Tyenne (Tocilizumab), in accordance with the national requirements, via the national spontaneous reporting system, to:

Boston Oncology Arabia Limited

King Abdelaziz Street, 11562, Riyadh, Saudi Arabia

PHONE: 011 245 5311

MOBILE: +966 547 643 672

E-MAIL: pv@bostononcology.com

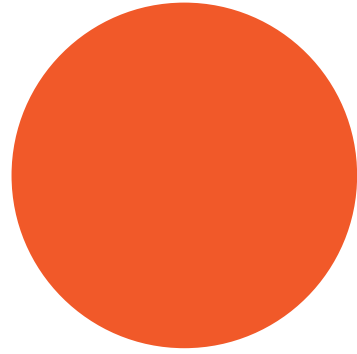
The National Pharmacovigilance Centre (NPC)

SFDA CALL CENTER: 19999

E-MAIL: npc.drug@sfda.gov.sa

WEBSITE: <http://ade.sfda.gov.sa/>

For full information on all possible side effects please see the Tyenne Package Leaflet.



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