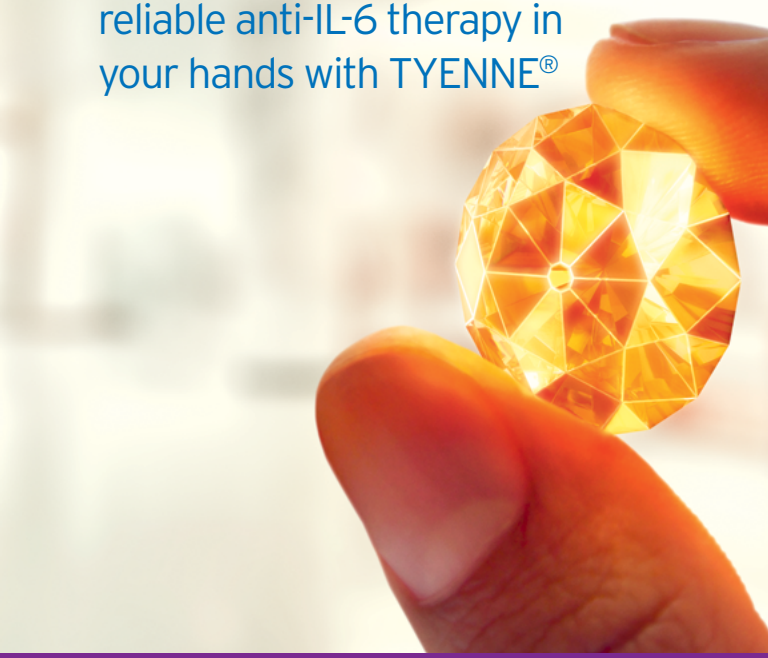
Tyenne®
tocilizumab-aazg

FDA-Approved Biosimilar to Actemra® (tocilizumab) with three administration options

Put the many facets of reliable anti-IL-6 therapy in your hands with TYENNE®



INDICATIONS

TYENNE is indicated for the treatment of:

Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs).

Giant cell arteritis (GCA) in adult patients.

Active polyarticular juvenile idiopathic arthritis (PJIA) in patients 2 years of age and older.

Active systemic juvenile idiopathic arthritis (SJIA) in patients 2 years of age and older.

Important Safety Information

RISK OF SERIOUS INFECTIONS:

Patients treated with TYENNE® (tocilizumab-aazg) are at increased risk for developing serious infections that may lead to hospitalization or death, including tuberculosis (TB), bacterial, invasive fungal, viral, or other opportunistic infections. If a serious infection develops, interrupt TYENNE until the infection is controlled.

Please see Important Safety Information throughout this brochure and click to see full Prescribing Information, including **Boxed Warning** for TYENNE® (tocilizumab-aazg).

FRESENIUS KABI

FDA-APPROVED

TYENNE® (tocilizumab-aazg) met and exceeded FDA requirements for biosimilarity[1-5]:

FDA-approved based on proven similarity to Actemra® (tocilizumab) in[1-5]:

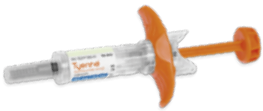
- Pharmacokinetic (PK) and pharmacodynamic (PD) profiles
- Efficacy
- Safety and immunogenicity

TYENNE® has been studied in a **Phase III study, including a switching arm** in patients with RA[3].

Available in the same three administration options as Actemra®[5]

Prefilled Autoinjector

162 mg/0.9 mL
NDC# 65219-0584-01



Prefilled Syringe

162 mg/0.9 mL
NDC# 65219-0586-04

IV Vials

80 mg/4 mL
NDC# 65219-0590-04

200 mg/10 mL
NDC# 65219-0592-10

400 mg/20 mL
NDC# 65219-0594-20

For RA, PJIA, and SJIA, TYENNE® can be taken with or without disease-modifying antirheumatic drugs (DMARDs), like methotrexate.*

*Not recommended for concomitant use with biological DMARDs.

Important Safety Information (continued)

Reported infections include:

- **Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before TYENNE use and during therapy. Treatment for latent infection should be initiated prior to TYENNE use.**
- **Invasive fungal infections, including candidiasis, aspergillosis, and pneumocystis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.**
- **Bacterial, viral and other infections due to opportunistic pathogens.**

The risks and benefits of treatment with TYENNE should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with TYENNE, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

CONTRAINDICATION

TYENNE is contraindicated in patients with known hypersensitivity to tocilizumab products.

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ENHANCED ADMINISTRATION FEATURES

Prefilled autoinjector for subcutaneous (SC) injection[5]

Rather than a separate injection button, the TYENNE® prefilled autoinjector uses a simple "push-on skin" activation mechanism for administration.[5]

Device Features[6]	TYENNE® (tocilizumab-aazg) Autoinjector	Actemra® (tocilizumab) Autoinjector
36-month product shelf life	✓	30 months
2-step sleeve activated	✓	
Four-sided, non-roll barrel	✓	
Manual needle insertion & retraction	✓	
Hold for up to 10 seconds to administer	✓	✓
27-gauge special thin-walled needle	✓	
Autoinjector with passive needle guard	✓	✓

Prefilled syringe for subcutaneous (SC) injection[5]

With extended finger flanges for stability and a safety needle guard to protect patients and caregivers, TYENNE® prefilled syringe can provide a simple, enhanced administration option.

Device Features[6]	TYENNE® (tocilizumab-aazg) Syringe	Actemra® (tocilizumab) Syringe
36-month product shelf life	✓	30 months
Clear needle guard	✓	✓
27-gauge special thin-walled needle	✓	
Liquid-filled syringe barrel	✓	✓
Extended finger flanges	✓	

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS

Gastrointestinal Perforations

Events of gastrointestinal (GI) perforation have been reported in clinical trials, primarily as complications of diverticulitis in patients treated with tocilizumab. Use TYENNE with caution in patients who may be at increased risk for GI perforation. Promptly evaluate patients presenting with new-onset abdominal symptoms for early identification of GI perforation.

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ADMINISTRATION AND DOSING

Same weight-based dosing as Actemra® (tocilizumab)[5]

Prefilled autoinjector and prefilled syringe for subcutaneous injection

Indication	Patient Weight	Dose
RA	< 100 kg	162 mg administered subcutaneously every other week, followed by an increase to every week based on clinical response
	≥ 100 kg	162 mg administered subcutaneously every week
GCA	The recommended dose is 162 mg given once every week as a subcutaneous injection, in combination with a tapering course of glucocorticoids. A dose of 162 mg given once every other week, in combination with a tapering course of glucocorticoids, may be prescribed based on clinical considerations	
PJIA	< 30 kg	162 mg once every 3 weeks
	≥ 30 kg	162 mg once every 2 weeks
SJIA	< 30 kg	162 mg once every 2 weeks
	≥ 30 kg	162 mg once every week

Follow the instructions for use for the prefilled autoinjector and prefilled syringe

Vials for IV infusion

The duration of the infusion typically lasts one hour.

Indication	Dose per kg of body weight	Dosing frequency
Adult RA	4 mg/kg followed by an increase to 8 mg/kg based on clinical response	Every 4 weeks
Adult GCA[a]	6 mg/kg	Every 4 weeks
PJIA (≥30 kg of body weight)	8 mg/kg	Every 4 weeks
PJIA (<30 kg of body weight)	10 mg/kg	Every 4 weeks
SJIA (≥30 kg of body weight)	8 mg/kg	Every 2 weeks
SJIA (<30 kg of body weight)	12 mg/kg	Every 2 weeks

IV=intravenous; RA=rheumatoid arthritis; GCA=giant cell arteritis; PJIA=polyarticular juvenile idiopathic arthritis; SJIA=systemic juvenile idiopathic arthritis.
[a]In combination with a tapering course of glucocorticoids. TYENNE® can be used alone after discontinuation of glucocorticoids.

Scan the QR code to determine a patient's correct dose using the TYENNE® IV dosing calculator.

Important Safety Information (continued)

Hepatotoxicity

Serious cases of hepatic injury have been observed in patients taking intravenous or subcutaneous tocilizumab products. Some of these cases have resulted in liver transplant or

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KabiCare

Patient support from Fresenius Kabi

KabiCare provides comprehensive patient support to enable patient access

- **Centralized patient support portal**
- **Financial support, including copay assistance***
- **Dedicated Access Specialists**
- **Bridge to Therapy program†**
- **Nurse educators‡**
- **Patient and provider education**
- **Clinical Insights Program§||**

With KabiCare, eligible patients prescribed TYENNE® may be able to pay as little as $0/month in out-of-pocket costs*

To learn more about the the KabiCare patient support program, visit **KabiCare.us**, scan the QR code, or call **1.833.KABICARE (1-833-522-4227).**

TYENNE® offers additional educational tools and resources, including:

- Sampling
- Educational resources
- Video resources
- Demo kits

* Eligibility criteria apply. Patients are not eligible for commercial copay support if the prescription is eligible to be reimbursed, in whole or part, by any state or federal healthcare program.

† Eligibility criteria apply. Patients are not eligible for the Bridge to Therapy program if the prescription is eligible to be reimbursed, in whole or in part, by any state or federal healthcare program.

‡ Nurse support provided by KabiCare is not meant to replace discussions with a healthcare provider regarding a care and treatment.

§ Patients must be 18 years or older and prescribed TYENNE for an on-label indication. Patients are not eligible for the Clinical Insights Program if the prescription is eligible to be reimbursed, in whole or in part, by any state or federal healthcare program.

|| The Clinical Insights Anser Tests were developed and validated by Prometheus Laboratories, Inc., a partner of Fresenius Kabi. Test results are provided via Prometheus Laboratories Inc., to physicians. Prescribing physicians are decision makers and are ultimately responsible for the exercise of independent clinical judgment in the best interest of patients.

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FRESENIUS KABI BIOSIMILARS

At Fresenius Kabi, our global expertise in complex medicine, state-of-the-art supply chain, and manufacturing allows us to deliver consistent quality biosimilars.[6]

A strong history of scientific expertise, quality manufacturing, and reliable supply

Multiple additional biosimilars in development

TYENNE® (tocilizumab-aazg) is produced in an FDA-inspected European facility with **over 20 years of experience manufacturing biologics**

Awards: Vizient 2022 Pharmaceutical Supplier Partner of the Year and Premier Supplier Legacy Award[7]

Important Safety Information (continued)

death. Time to onset for cases ranged from months to years after treatment initiation. Most cases presented with marked elevations of transaminases (> 5 times ULN), and some cases presented with signs or symptoms of liver dysfunction and only mildly elevated transaminases.

Treatment with tocilizumab was associated with a higher incidence of transaminase elevations; increased frequency and magnitude of these elevations were observed when tocilizumab was used in combination with potentially hepatotoxic drugs (e.g., methotrexate).

It is not recommended to initiate TYENNE treatment in RA, GCA, PJIA, and SJIA patients with elevated transaminases ALT or AST greater than 1.5x ULN. In patients who develop elevated ALT or AST greater than 5x ULN discontinue TYENNE.

Measure liver tests promptly in patients who report symptoms that may indicate liver injury. If the patient is found to have abnormal liver tests, TYENNE treatment should be interrupted. TYENNE should only be restarted in patients with another explanation for the liver test abnormalities after normalization of the liver tests.

Laboratory Parameters

Laboratory monitoring is recommended due to potential consequences of treatment-related laboratory abnormalities in neutrophils, platelets, lipids, and liver function tests. Dosage modifications may be required.

Neutropenia: Treatment with tocilizumab products was associated with a higher incidence of neutropenia. It is not recommended to initiate TYENNE treatment in RA, GCA, PJIA, and SJIA patients with a low neutrophil count i.e., absolute neutrophil count (ANC) less than 2000 per mm^3. In patients who develop an ANC less than 500 per mm^3 treatment is not recommended.

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Important Safety Information (continued)

Thrombocytopenia: Treatment with tocilizumab products was associated with a reduction in platelet counts. It is not recommended to initiate TYENNE in RA, GCA, PJIA, and SJIA patients with a platelet count below 100,000 per mm^3. In patients who develop a platelet count less than 50,000 per mm^3, treatment is not recommended.

Elevated Liver Enzymes: It is not recommended to initiate TYENNE treatment in patients with elevated transaminases ALT or AST >1.5x ULN. In patients who develop elevated ALT or AST >5x ULN, treatment is not recommended.

Lipid Abnormalities: Treatment with tocilizumab products was associated with increases in lipid parameters such as total cholesterol, triglycerides, LDL cholesterols, and/or HDL cholesterol.

Immunosuppression

The impact of treatment with tocilizumab products on the development of malignancies is not known, but malignancies were observed in clinical studies with tocilizumab. TYENNE is an immunosuppressant, and treatment with immunosuppressants may result in an increased risk of malignancies.

Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis, have been reported in association with tocilizumab products and anaphylactic events with a fatal outcome have been reported with intravenous infusion of tocilizumab products. TYENNE for intravenous use should only be infused by a healthcare professional with appropriate medical support to manage anaphylaxis. For TYENNE subcutaneous injection, advise patients to seek immediate medical attention if they experience any symptoms of a hypersensitivity reaction. If anaphylaxis or other hypersensitivity reaction occurs, stop administration of TYENNE immediately and discontinue TYENNE permanently. Do not administer TYENNE to patients with known hypersensitivity to tocilizumab products.

Demyelinating Disorders
The impact of treatment with tocilizumab products on demyelinating disorders is not known, but multiple sclerosis and chronic inflammatory demyelinating polyneuropathy were reported rarely in clinical studies. Monitor patients for signs and symptoms of demyelinating disorders. Prescribers should exercise caution in considering the use of TYENNE in patients with preexisting or recent-onset demyelinating disorders.

Active Hepatic Disease and Hepatic Impairment

Treatment with TYENNE is not recommended in patients with active hepatic disease or hepatic impairment.

Vaccinations

Avoid use of live vaccines concurrently with TYENNE. No data are available on the secondary transmission of infection from persons receiving live vaccines to patients receiving TYENNE or on the effectiveness of vaccination in patients receiving TYENNE. Patients should be brought up to date on all recommended vaccinations prior to initiation of TYENNE therapy, if possible.

ADVERSE REACTIONS

Most common adverse reactions (incidence of at least 5%): upper respiratory tract infections, nasopharyngitis, headache, hypertension, increased ALT, injection site reactions.

DRUG INTERACTIONS

In GCA patients, no effect of concomitant corticosteroid on tocilizumab exposure was observed.

Cytochrome P450s in the liver are down-regulated by infection and inflammation stimuli including cytokines such as IL-6. Inhibition of IL-6 signaling in RA patients treated with tocilizumab products may restore CYP450 activities to higher levels than those in the absence of tocilizumab products leading to increased metabolism of drugs that are CYP450 substrates.

Exercise caution when coadministering TYENNE with CYP3A4 substrate drugs where decrease in effectiveness is undesirable, e.g., oral contraceptives, lovastatin, atorvastatin, etc.

USE IN PREGNANCY

The limited available data with tocilizumab products in pregnant women are not sufficient to determine whether there is a drug-associated risk for major birth defects and miscarriage.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Fresenius Kabi at (800) 551-7176.

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Experience the many facets of biosimilar anti-IL-6 therapy with TYENNE® (tocilizumab-aazg)

- **FDA-approved for RA, SJIA, PJIA, and GCA, similar to Actemra® (tocilizumab)[5]**
- **No clinically meaningful differences to Actemra®[1-4]**
- **TYENNE® SC demonstrated equivalent efficacy to Actemra® SC[3]**
- **A tocilizumab biosimilar with all three Actemra® administration options: prefilled autoinjector, prefilled syringe, and IV infusion vials[5]**
- **Fresenius Kabi has a strong history of scientific expertise, quality manufacturing, and reliable supply**

KabiCare
Patient support from Fresenius Kabi

Comprehensive patient support, including educational, financial, and therapy resources

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References: 1. Schwabe C, Illes A, Ullmann M, et al. Pharmacokinetics and pharmacodynamics of a proposed tocilizumab biosimilar TYENNE® versus both the US-licensed and EU-approved products: a randomized, double-blind trial. *Expert Rev Clin Immunol*. 2022;18(5):533-543. **2.** Tomaszewska-Kiecana M, Dryja A, Ullmann M, et al. Pharmacokinetics and tolerability of prefilled syringe and auto-injector presentations of TYENNE®: results of a randomized, single-dose study in healthy adults. *Expert Rev Clin Immunol*. 2023;19(4):447-455. **3.** Zubrzycka-Sienkiewicz A, Klama K, Ullmann M, et al. Comparison of the efficacy and safety of a proposed biosimilar TYENNE with tocilizumab reference product in subjects with moderate-to-severe rheumatoid arthritis: results of a randomised double-blind study. *RMD Open*. 2024;10:e003596.doi:10.1136rmdopen-2023-003596. **4.** Tomaszewska-Kiecana M, Ullmann M, Petit-Frere C, et al. Pharmacokinetics of a proposed tocilizumab biosimilar (TYENNE) versus US-licensed tocilizumab: results of a randomized, double-blind, single-intravenous dose study in healthy adults. *Expert Rev Clin Immunol*. 2023;19(4):439-446. doi:10.1080/1744666X.2023.2174104 **5.** TYENNE. Package insert. Fresenius Kabi USA, LLC 2024. **6.** Data on file. Fresenius Kabi **7.** Fresenius Kabi. Fresenius Kabi named 2022 pharmaceutical supplier partner of the year by Vizient. Published October 6, 2022. Accessed January 9, 2024. https://www.fresenius-kabi.com/us/news/fresenius-kabi-named-2022-pharmaceutical-supplier-partner

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