Prescribing Information

Prescribing Information.Tyenne®▼(tocilizumab). This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Tocilizumab 20mg/mL concentrate for solution for infusion (vial of 4mL,10mL and 20mL), 162mg solution for injection in pre-filled pen and 162mg solution for injection in pre-filled syringe. Consult the Summary of Product Characteristics SmPC) before prescribing. Additional information is available on request. **Presentations and Active Ingredients:** Each pre-filled syringe and pre-filled pen contains 162mg of tocilizumab in 0.9mL. EachmL concentrate for solution for infusion contains 20mg tocilizumab. **Indication:** ***Rheumatoid arthritis (RA), adults [In combination with methotrexate (MTX)]:*** *Severe, active and progressive RA:* In patients not previously treated with MTX. *Moderate to severe active RA:* In patients who have either responded inadequately to, or who were intolerant to, previous disease-modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) antagonists. Can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate. ***Active systemic juvenile idiopathic arthritis (sJIA):*** *20mg/ml concentrate for Solution for Infusion:* In patients ≥ 2 years, who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids. 162mg solution for injection in Prefilled syringe: In patients ≥ 1 year, who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids. *162mg solution for injection in Pre-filled pen:* In patients ≥ 12 years who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids. Can be given as monotherapy (in case of intolerance to MTX or where treatment with MTX is inappropriate) or in combination with MTX. ***Juvenile idiopathic arthritis (pJIA; rheumatoid factor positive or negative and extended oligoarthritis):*** *20mg/ml concentrate for Solution for Infusion & 162mg solution for injection in Pre-filled syringe:* In combination with MTX in patients ≥ 2 years, who have responded inadequately to previous therapy with MTX. *162mg solution for injection in Pre-filled pen:* In combination with MTX in patients ≥ 12 years, who have responded inadequately to previous therapy with MTX. Can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate. ***Chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS):*** *20mg/ml concentrate for Solution for Infusion:* In adults and paediatric patients ≥ 2 years. ***Coronavirus disease 2019 (COVID-19), adults:*** *20mg/ml Concentrate for Solution for Infusion:* In patients receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation. ***Giant Cell Arteritis (GCA), adults:*** *162mg Solution for Injection in Pre-Filled Syringe & Pre-Filled Pen.* **Dosage:** ***20mg/ml Concentrate for Solution for Infusion:*** *RA: 8mg/kg, given once every 4 weeks. If bodyweight > 100 kg, doses above 800mg per infusion are not recommended. sJIA: ≥ 2 years and older: 8mg/kg once every 2 weeks if ≥ 30 kg & 12mg/kg once every 2 weeks if < 30 kg. pJIA: ≥ 2 years and older: 8mg/kg every 4 weeks if ≥ 30 kg & 10mg/kg every 4 weeks if < 30 kg. CRS: 8mg/kg* over 60 minutes if ≥ 30 kg; 12mg/kg over 60 minutes if < 30 kg. COVID-19: Single 60-minute intravenous infusion of 8mg/kg. ***162mg solution for injection in Pre-filled syringe:*** *RA:* 162mg once every week. *sJIA:* ≥ 1 year and older: *162mg once every week if ≥ 30 kg & 162mg once every 2 weeks if < 30 kg. pJIA: ≥ 2 years and older: 162mg once every 2 weeks if ≥ 30 kg & 162mg once every 3 weeks if < 30 kg. GCA:* 162mg once every week in combination with tapering course of glucocorticoids. ***162mg solution for injection in Pre-filled pen:*** *RA:* 162mg once every week. *sJIA:* ≥12 years of age: 162mg subcutaneously once every week if ≥ 30 kg & 162mg subcutaneously once every 2 weeks if < 30 kg. *pJIA: ≥ 12 years of age: 162mg subcutaneously once every 2 weeks if ≥ 30 kg & 162mg subcutaneously once every 3 weeks if < 30 kg. GCA:* 162mg once every week in combination with tapering course of glucocorticoids. Patients must have a minimum body weight of 10 kg when receiving TYENNE subcutaneously. The pre-filled pen should not be used to treat paediatric patients <12 years of age. **Contraindications:** Hypersensitivity to the active substance or to any excipients (see SmPC). Active, severe infections with the exception of COVID-19 in 20mg/ml concentrate for Solution or Infusion. **Warnings and Precautions:** In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. Serious and sometimes fatal infections have been reported in patients receiving immunosuppressive agents including tocilizumab. Tyenne treatment must not be initiated in patients with active infections and should be interrupted if serious infection develops until the infection is controlled. Caution to be exercised in patients with a history of recurring or chronic infections or with underlying conditions (e.g.) diverticulitis, diabetes and interstitial lung disease which may predispose patients to infections. Vigilance for timely detection of serious infection is recommended. Effects of tocilizumab on C-reactive protein (CRP), neutrophils and signs and symptoms of infection should be considered when evaluating a patient for a potential infection. For rapid evaluation and appropriate treatment, patients (including young children) and parents/guardians, should be instructed to contact their healthcare professional immediately when any symptoms suggesting infection appear. All patients should be screened for latent TB infection and in case of latent TB should be treated with standard antimycobacterial therapy before initiating tocilizumab. Risk of false negative tuberculin skin and interferon-gamma TB blood test results, especially in patients who are severely ill or immunocompromised seek medical advice if signs/symptoms (e.g., persistent cough, wasting/weight loss, low grade (fever) suggestive of a TB infection occur during or after therapy with Tyenne. Viral reactivation (e.g. hepatitis B virus) has been reported with biologic therapies for RA. Diverticular perforations have been reported uncommonly in patients treated with tocilizumab. Patients presenting with symptoms such as abdominal pain, haemorrhage and/or unexplained change in bowel habits with fever should be evaluated promptly. Reports of serious allergic reactions including anaphylaxis received. For serious allergic or anaphylactic reactions, stop Tyenne immediately and discontinue treatment and initiate appropriate therapy. Caution should be exercised when considering treatment of patients with active hepatic disease or hepatic impairment. Elevations of hepatic transaminases have been reported. Serious drug-induced liver injury, including acute liver failure resulting in liver transplantation, hepatitis and jaundice, have been observed. Patients should be advised to immediately seek medical help if they experience signs and symptoms of hepatic injury. Caution in patients with elevated ALT or AST > 1.5 x ULN; interrupted treatment or ALT or AST elevations > 3–5 x ULN and not recommended in patients with baseline ALT or AST > 5 x ULN. ALT/AST should be monitored every 4 to 8 weeks for the first 6 months of treatment followed by every 12 weeks thereafter.

Decreases in neutrophil and platelet counts reported with tocilizumab 8mg/kg in combination with MTX. Treatment initiation is not recommended in patients with an ANC below 2 x 109/L. Caution in patients with platelet count below 100 x 103/µL. Discontinue when ANC < 0.5 x 109/L or a platelet count < 50 x 103/µL. Neutrophils and platelets should be monitored. Elevations in lipid parameters including total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides reported. Assessment of lipid parameters 4 to 8 weeks following initiation of tocilizumab therapy recommended. Physicians should be vigilant for symptoms potentially indicative of new-onset central demyelinating disorders. Risk of malignancy is increased in patients with RA. Immunomodulatory medicinal products may increase the risk of malignancy. Live and live attenuated vaccines should not be given concurrently with tocilizumab. Interval between live vaccinations and initiation of tocilizumab therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. Increased risk for cardiovascular disorders. Risk factors (e.g. hypertension, hyperlipidaemia) managed as part of the usual standard of care. Not recommended for use with other biological agents. Tocilizumab monotherapy should not be used for the treatment of acute relapses in GCA. Glucocorticoids should be given according to medical judgement and practice guidelines. Serious life-threatening disorder, macrophage activation syndrome (MAS) may develop in sJIA patients. Tocilizumab is not studied in patients during an episode of active MAS. The medicinal product contains sodium. To be taken into consideration by patients on a controlled sodium diet. Efficacy of tocilizumab solution for infusion has not been established in the treatment of COVID-19 patients who do not have elevated CRP levels. Should not be administered to COVID-19 patients if they have any other concurrent severe active infection and who are not receiving systemic corticosteroids. **Interactions:** Interaction studies have only been performed in adults. Concomitant administration of a single dose of 10mg/kg tocilizumab with 10-25mg MTX once weekly had no clinically significant effect on MTX exposure. No effect of MTX, non-steroidal anti-inflammatory drugs (NSAIDs) or corticosteroids on tocilizumab clearance in RA patients. In GCA patients, no effect of cumulative corticosteroid dose on tocilizumab exposure was observed. CYP450 expression may be reversed when potent cytokine inhibitory therapy, such as tocilizumab, is introduced. Tocilizumab normalises expression of CYP1A2, CYP2C9, CYP2C19, and CYP3A4 enzyme enzymes. Medicines metabolised via CYP450 3A4, 1A2 or 2C9 (e.g. methylprednisolone, dexamethasone, (with the possibility for oral glucocorticoid withdrawal syndrome), atorvastatin, calcium channel blockers, theophylline, warfarin, phenprocoumon, phenytoin, ciclosporin, or benzodiazepines) should be monitored when starting or stopping therapy with tocilizumab, as doses may need to be increased to maintain therapeutic effect. Given its long elimination half-life (t1/2), the effect of tocilizumab on CYP450 enzyme activity may persist for several weeks after stopping therapy. **Pregnancy and lactation:** Tyenne should not be used during pregnancy unless clearly necessary. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with Tyenne should be made taking into account the benefit of breast-feeding to the child and the benefit of tocilizumab therapy to the woman **Adverse Reactions:** Very common ≥ 1/10: Upper respiratory tract infections, hypercholesterolaemia, injection site reaction. Common ≥ 1/100 to < 1/10: Cellulitis, pneumonia, oral herpes simplex, herpes zoster, leukopenia, neutropenia, hypofibrinogenaemia, headache, dizziness, conjunctivitis, hypertension, cough, dyspnoea, abdominal pain, mouth ulceration, gastritis, rash, pruritus, urticaria, peripheral oedema, hypersensitivity reactions, hepatic transaminases increased, weight increased, total bilirubin increased. Fatal anaphylaxis, drug-induced liver injury, hepatitis, jaundice, rare hepatic failure, Stevens-Johnson-Syndrome are serious side effects reported. There have been post-marketing reports of interstitial lung disease (including pneumonitis and pulmonary fibrosis), some of which had fatal outcomes. Other less common and rarely reported adverse reactions are listed in the SmPC. **Pack Sizes:** ***Ireland:*** *Pack quantities and costs:* 162mg pre-filled syringe: Pack size 4 (€531.65); 162mg pre-filled pen: Pack size 4 (€531.65); 200mg/10mL conc for sol: Pack size 1 (€183.84); 400mg/20mL conc for sol: Pack size 1 (€365.66); 80mg/4mL conc for sol: Pack size 1 (€73.49). ***United Kingdom:*** *Pack quantities and costs:* 162mg pre-filled syringe: Pack size 4 (£821.81); 162mg pre-filled pen: Pack size 4 (£821.81); 200mg/10mL solution for infusion vials: Pack size 1 (£230.40); 400mg/20mL solution for infusion vials: Pack size 1 (£460.80); 80mg/4mL solution for infusion vials: Pack size 1 (£92.16). **Legal Category:** POM. **Marketing Authorisation Numbers:** ***Ireland:*** 162mg pre-filled pen: EU/1/23/1754/011; 162mg Prefilled syringe: EU/1/23/1754/008; 20mg/mL concentrate: (4mL vial): EU/1/23/1754/001; (10mL vial): EU/1/23/1754/003; (20mL vial): EU/1/23/1754/005. ***United Kingdom:*** 162mg pre-filled pen: PLGB 08828/0357; 162mg pre-filled syringe: PLGB 08828/0358; 20mg/mL concentrate: (4mL, 10mL & 20mLvial): PLGB 08828/0359. **Marketing Authorisation Holder:** Fresenius Kabi Deutschland GmbH, Else- Kroener-Strasse 1, 61352 Bad Homburg v.d. Hoehe, Germany. GB Marketing Authorisation Holder: Fresenius Kabi Ltd, Cestrian Court, Eastgate Way, Manor Park, Runcorn, Cheshire, WA7 1NT, United Kingdom. **Further Information:** See the SmPC for further details.

Date of preparation: September 2023 | Job code: IE-TYE-2300023(a)

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FRESENIUS KABI

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Tyenne treatment must not be initiated in patients with active infections and should be interrupted if serious infection develops until the infection is controlled. Caution to be exercised in patients with a history of recurring or chronic infections or with underlying conditions (e.g.) diverticulitis, diabetes and interstitial lung disease which may predispose patients to infections. Vigilance for timely detection of serious infection is recommended. Effects of tocilizumab on C-reactive protein (CRP), neutrophils and signs and symptoms of infection should be considered when evaluating a patient for a potential infection. For rapid evaluation and appropriate treatment, patients (including young children) and parents/guardians, should be instructed to contact their healthcare professional immediately when any symptoms suggesting infection appear. All patients should be screened for latent TB infection and in case of latent TB should be treated with standard antimycobacterial therapy before initiating tocilizumab. Risk of false negative tuberculin skin and interferon-gamma TB blood test results, especially in patients who are severely ill or immunocompromised seek medical advice if signs/symptoms (e.g., persistent cough, wasting/weight loss, low grade (fever) suggestive of a TB infection occur during or after therapy with Tyenne. Viral reactivation (e.g. hepatitis B virus) has been reported with biologic therapies for RA. Diverticular perforations have been reported uncommonly in patients treated with tocilizumab. Patients presenting with symptoms such as abdominal pain, haemorrhage and/or unexplained change in bowel habits with fever should be evaluated promptly. Reports of serious allergic reactions including anaphylaxis received. For serious allergic or anaphylactic reactions, stop Tyenne immediately and discontinue treatment and initiate appropriate therapy. Caution should be exercised when considering treatment of patients with active hepatic disease or hepatic impairment. Elevations of hepatic transaminases have been reported. Serious drug-induced liver injury, including acute liver failure resulting in liver transplantation, hepatitis and jaundice, have been observed. Patients should be advised to immediately seek medical help if they experience signs and symptoms of hepatic injury. Caution in patients with elevated ALT or AST > 1.5 x ULN; interrupted treatment or ALT or AST elevations > 3–5 x ULN and not recommended in patients with baseline ALT or AST > 5 x ULN. ALT/AST should be monitored every 4 to 8 weeks for the first 6 months of treatment followed by every 12 weeks thereafter. Decreases in neutrophil and platelet counts reported with tocilizumab 8mg/kg in combination with MTX. Treatment initiation is not recommended in patients with an ANC below 2 x 109/L. Caution in patients with platelet count below 100 x 103/µL. Discontinue when ANC < 0.5 x 109/L or a platelet count < 50 x 103/µL. Neutrophils and platelets should be monitored. Elevations in lipid parameters including total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides reported. Assessment of lipid parameters 4 to 8 weeks following initiation of tocilizumab therapy recommended. Physicians should be vigilant for symptoms potentially indicative of new-onset central demyelinating disorders. Risk of malignancy is increased in patients with RA. Immunomodulatory medicinal products may increase the risk of malignancy. Live and live attenuated vaccines should not be given concurrently with tocilizumab. Interval between live vaccinations and initiation of tocilizumab therapy should be in accordance with current vaccination guidelines regarding immunosuppressive agents. Increased risk for cardiovascular disorders. Risk factors (e.g. hypertension, hyperlipidaemia) managed as part of the usual standard of care. Not recommended for use with other biological agents. Tocilizumab monotherapy should not be used for the treatment of acute relapses in GCA. Glucocorticoids should be given according to medical judgement and practice guidelines. Serious life-threatening disorder, macrophage activation syndrome (MAS) may develop in sJIA patients. Tocilizumab is not studied in patients during an episode of active MAS. The medicinal product contains sodium. To be taken into consideration by patients on a controlled sodium diet. Efficacy of tocilizumab solution for infusion has not been established in the treatment of COVID-19 patients who do not have elevated CRP levels. Should not be administered to COVID-19 patients if they have any other concurrent severe active infection and who are not receiving systemic corticosteroids. **Interactions:** Interaction studies have only been performed in adults. Concomitant administration of a single dose of 10mg/kg tocilizumab with 10-25mg MTX once weekly had no clinically significant effect on MTX exposure. No effect of MTX, non-steroidal anti-inflammatory drugs (NSAIDs) or corticosteroids on tocilizumab clearance in RA patients. In GCA patients, no effect of cumulative corticosteroid dose on tocilizumab exposure was observed. CYP450 expression may be reversed when potent cytokine inhibitory therapy, such as tocilizumab, is introduced. Tocilizumab normalises expression of CYP1A2, CYP2C9, CYP2C19, and CYP3A4 enzyme enzymes. Medicines metabolised via CYP450 3A4, 1A2 or 2C9 (e.g. methylprednisolone, dexamethasone, (with the possibility for oral glucocorticoid withdrawal syndrome), atorvastatin, calcium channel blockers, theophylline, warfarin, phenprocoumon, phenytoin, ciclosporin, or benzodiazepines) should be monitored when starting or stopping therapy with tocilizumab, as doses may need to be increased to maintain therapeutic effect. Given its long elimination half-life (t1/2), the effect of tocilizumab on CYP450 enzyme activity may persist for several weeks after stopping therapy. **Pregnancy and lactation:** Tyenne should not be used during pregnancy unless clearly necessary. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with Tyenne should be made taking into account the benefit of breast-feeding to the child and the benefit of tocilizumab therapy to the woman **Adverse Reactions:** Very common ≥ 1/10: Upper respiratory tract infections, hypercholesterolaemia, injection site reaction. Common ≥ 1/100 to < 1/10: Cellulitis, pneumonia, oral herpes simplex, herpes zoster, leukopenia, neutropenia, hypofibrinogenaemia, headache, dizziness, conjunctivitis, hypertension, cough, dyspnoea, abdominal pain, mouth ulceration, gastritis, rash, pruritus, urticaria, peripheral oedema, hypersensitivity reactions, hepatic transaminases increased, weight increased, total bilirubin increased. Fatal anaphylaxis, drug-induced liver injury, hepatitis, jaundice, rare hepatic failure, Stevens-Johnson-Syndrome are serious side effects reported. 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Hoehe, Germany. GB Marketing Authorisation Holder: Fresenius Kabi Ltd, Cestrian Court, Eastgate Way, Manor Park, Runcorn, Cheshire, WA7 1NT, United Kingdom. **Further Information:** See the SmPC for further details.

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Fresenius Kabi Ltd. Cestrian Court, Eastgate Way,
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