

PRODUCT MONOGRAPH  
INCLUDING PATIENT MEDICATION INFORMATION

**PrTREMIFYA®**  
guselkumab injection  
Solution for injection,  
100 mg/1 mL  
Pre-filled syringe

**PrTREMIFYA One-Press®**  
guselkumab injection  
Solution for injection,  
100 mg/1 mL  
Patient-controlled injector  
Interleukin-23 (IL-23) inhibitor

TREMIFYA®/TREMIFYA One-Press® (guselkumab injection) should be prescribed by physicians who have sufficient knowledge of plaque psoriasis or psoriatic arthritis and who have fully familiarized themselves with the efficacy/safety profile of the drug.

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## RECENT MAJOR LABEL CHANGES

None at the time of the most recent authorization.

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Sections or subsections that are not applicable at the time of authorization are not listed.

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## **PART I: HEALTH PROFESSIONAL INFORMATION**

### **1 INDICATIONS**

#### **Plaque Psoriasis**

TREMFYA®/TREMFYA One-Press® (guselkumab injection) is indicated for:

- the treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

#### **Psoriatic Arthritis**

TREMFYA®/TREMFYA One-Press® (guselkumab injection) is indicated for:

- the treatment of adult patients with active psoriatic arthritis. TREMFYA®/TREMFYA One-Press® can be used alone or in combination with a conventional disease-modifying antirheumatic drug (cDMARD) (e.g., methotrexate).

#### **1.1 Pediatrics**

The safety and efficacy of TREMFYA®/TREMFYA One-Press® in pediatric patients have not been evaluated.

#### **1.2 Geriatrics**

Of the 3406 plaque psoriasis and psoriatic arthritis patients exposed to TREMFYA®/TREMFYA One-Press® in Phase 2 and Phase 3 clinical trials, a limited number of patients were 65 years or older (n = 185, 5%) or 75 years and older (n=13, 0.4%). Thus, data in these age groups are limited (see [10 CLINICAL PHARMACOLOGY](#)).

### **2 CONTRAINDICATIONS**

TREMFYA®/TREMFYA One-Press® is contraindicated in patients with known serious hypersensitivity to guselkumab or any of the components. For a complete listing of components, see the [6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING](#) section.

### **4 DOSAGE AND ADMINISTRATION**

TREMFYA®/TREMFYA One-Press® is administered by subcutaneous injection.

#### **4.1 Dosing Considerations**

TREMFYA®/TREMFYA One-Press® is intended for use under the guidance and supervision of a physician.

TREMFYA®/TREMFYA One-Press® may be administered by a healthcare professional, or a patient or caregiver may administer the injection after proper training in subcutaneous injection technique.

#### **4.2 Recommended Dose and Dosage Adjustment**

##### **Plaque psoriasis**

The recommended dose of TREMFYA®/TREMFYA One-Press® is 100 mg to be given as

subcutaneous injection at week 0 and week 4, followed by maintenance dosing every 8 weeks thereafter.

### **Psoriatic arthritis**

The recommended dose of TREMFYA®/TREMFYA One-Press® is 100 mg to be given as subcutaneous injection at week 0 and week 4, followed by maintenance dosing every 8 weeks thereafter.

TREMFYA®/TREMFYA One-Press® can be used alone or in combination with a conventional disease-modifying antirheumatic drug (cDMARD) (e.g., methotrexate).

### **Special populations**

#### **Pediatrics (< 18 years of age)**

The safety and efficacy of TREMFYA®/TREMFYA One-Press® in pediatric patients have not been evaluated; therefore, no recommendations on dosing can be made.

#### **Elderly (≥ 65 years of age)**

Of the 3406 plaque psoriasis and psoriatic arthritis patients exposed to TREMFYA®/TREMFYA One-Press® in Phase 2 and Phase 3 clinical trials, a limited number of patients were 65 years or older (n = 185, 5%) or 75 years and older (n=13, 0.4%). Thus, data in these age groups are limited (see [10 CLINICAL PHARMACOLOGY](#)).

#### **Renal impairment**

Specific studies of TREMFYA®/TREMFYA One-Press® have not been conducted in patients with renal insufficiency.

#### **Hepatic impairment**

Specific studies of TREMFYA®/TREMFYA One-Press® have not been conducted in patients with hepatic insufficiency.

## **4.4 Administration**

TREMFYA®/TREMFYA One-Press® is administered by subcutaneous injection. TREMFYA®/TREMFYA One-Press® is intended for use under the guidance and supervision of a physician. TREMFYA®/TREMFYA One-Press® may be administered by a healthcare professional or a patient or caregiver may administer the injection after proper training in subcutaneous injection technique.

The full amount of TREMFYA® /TREMFYA One-Press® should be injected according to the directions provided in the “Instructions for Use” document.

Before injection, remove TREMFYA®/TREMFYA One-Press® from the refrigerator and allow TREMFYA®/TREMFYA One-Press® to reach room temperature (30 minutes) without removing the needle cap.

Inspect TREMFYA®/TREMFYA One-Press® visually for particulate matter and discoloration prior to administration. TREMFYA®/TREMFYA One-Press® is a clear and colourless to light yellow solution. Do not use if the liquid contains large particles, is discoloured or cloudy. Discard any

unused product remaining after injection.

#### 4.5 Missed Dose

Patients who miss a dose of TREMFYA®/TREMFYA One-Press® should be advised to inject this missed dose as soon as they become aware of it, and then follow with their next scheduled dose.

#### 5 OVERDOSAGE

Single intravenous doses of TREMFYA® up to 987 mg (10 mg/kg) have been administered in healthy volunteers and single subcutaneous doses of TREMFYA® up to 300 mg have been administered in patients with plaque psoriasis in clinical trials without dose-limiting toxicity. In the event of overdosage, monitor the patient for any signs or symptoms of adverse reactions and administer appropriate symptomatic treatment immediately.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

#### 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of biologic products, including biosimilars, health professionals should recognize the importance of recording both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Subcutaneous Injection (SC)	Sterile solution for injection in pre-filled syringe, (100 mg/ 1 mL)	L-histidine, L-histidine monohydrochloride monohydrate, polysorbate 80, sucrose and water for injection
Subcutaneous Injection (SC)	Sterile solution for injection in a patient-controlled injector, (100 mg/ 1 mL)	L-histidine, L-histidine monohydrochloride monohydrate, polysorbate 80, sucrose and water for injection

TREMFYA®/TREMFYA One-Press® (guselkumab injection) is a fully human immunoglobulin G1 lambda (IgG1λ) monoclonal antibody (mAb) that binds selectively to the extracellular human interleukin 23 (IL-23) protein with high specificity and affinity. Guselkumab is produced in a mammalian cell line using recombinant DNA technology.

TREMFYA® is supplied as:

A sterile solution in a single-dose 1mL glass syringe with a 27G, half inch fixed needle assembled in a passive needle guard delivery system, containing 100 mg guselkumab, (100 mg/1 mL in a 1 mL syringe volume) packaged in a carton.

TREMFYA One-Press® is supplied as:

A sterile solution in a single-dose 1 mL glass syringe with a 27G, half inch fixed needle assembled in a patient-controlled injector containing 100 mg guselkumab, (100 mg/1 mL in a 1 mL volume) packaged in a carton.

TREMFYA®/TREMFYA One-Press® does not contain preservatives.

The TREMFYA®/TREMFYA One-Press® needle guard and plunger stopper are not made with natural rubber latex.

## 7 WARNINGS AND PRECAUTIONS

### General

#### ***Infections***

TREMFYA®/TREMFYA One-Press® is a selective immunomodulatory agent which has the potential to increase the risk of infection. Infections have been observed in clinical trials in plaque psoriasis (23% vs 21% for placebo; ≤ 0.2% serious infections in both groups) and psoriatic arthritis (21% in both TREMFYA® and placebo groups; ≤ 0.8% serious infections in both groups). The most common type of infection reported was respiratory tract infection. (See [8 ADVERSE REACTIONS](#), Infections)

Treatment with TREMFYA®/TREMFYA One-Press® should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated.

Instruct patients treated with TREMFYA®/TREMFYA One-Press® to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops a clinically important or serious infection or is not responding to standard therapy, monitor the patient closely and discontinue TREMFYA®/TREMFYA One-Press® until the infection resolves.

In clinical studies, subjects with latent tuberculosis (TB) who were concurrently treated with TREMFYA® and appropriate TB prophylaxis did not develop TB. Evaluate patients for TB infection prior to initiating treatment with TREMFYA®/TREMFYA One-Press®. Initiate treatment of latent TB prior to administering TREMFYA®/TREMFYA One-Press®. Patients receiving TREMFYA®/TREMFYA One-Press® should be monitored for signs and symptoms of active TB during and after treatment. Do not administer TREMFYA®/TREMFYA One-Press® to patients with active TB infection. Consider anti-TB therapy prior to initiating TREMFYA®/TREMFYA One-Press® in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed.

### Immune

#### ***Vaccinations***

Prior to initiating therapy with TREMFYA®/TREMFYA One-Press®, consider completion of all age appropriate immunizations according to current immunization guidelines. Avoid use of live vaccines in patients treated with TREMFYA®/TREMFYA One-Press® (see [9 DRUG INTERACTIONS](#)). No data are available on the response to live or inactive vaccines.

## Reproductive Health: Female and Male Potential

- **Fertility**

The effect of TREMFYA®/TREMFYA One-Press® on human fertility has not been evaluated. No guselkumab-related effects on fertility parameters were identified in a female fertility study conducted in guinea pigs. In a male guinea pig fertility study, total litter loss was observed in a limited subset of untreated females following administration of males with guselkumab at a subcutaneous dose of 100 mg/kg twice weekly (24-fold the human exposure). This observation was not repeated in a second male fertility study. No effects were observed at 25 mg/kg ( $C_{max}$  and  $AUC_{last}$  values were 51- and 6-fold greater, respectively, than the human exposure) (see [16 NON-CLINICAL TOXICOLOGY](#)).

## Sensitivity/Resistance

### Hypersensitivity

Serious hypersensitivity reactions, including anaphylaxis, have been reported in the postmarketing setting. Some serious hypersensitivity reactions occurred several days after treatment with TREMFYA®, including cases with urticaria and dyspnea. If a serious hypersensitivity reaction occurs, appropriate therapy should be instituted and administration of TREMFYA®/TREMFYA One-Press® should be discontinued.

## 7.1 Special Populations

### 7.1.1 Pregnant Women

The use of TREMFYA®/TREMFYA One-Press® in pregnant women has not been studied. The effect of TREMFYA®/TREMFYA One-Press® on human pregnancy is unknown. Studies in cynomolgus monkeys showed that guselkumab crosses the placental barrier. Fetal losses and neonatal deaths occurred in the offspring of pregnant monkeys administered weekly subcutaneous injections of guselkumab from the beginning of organogenesis until parturition at  $C_{max}$  and  $AUC_{last}$  values that were 31- and 8-fold greater, respectively, than the human levels. A drug-related effect could not be ruled out. No adverse developmental effects were observed in surviving infants. Animal studies are not always predictive of human response, and therefore, the clinical significance of these findings is unknown (see [16 NON-CLINICAL TOXICOLOGY](#)).

Women of childbearing potential should use adequate contraception while using TREMFYA®/TREMFYA One-Press® and for at least 12 weeks after the last TREMFYA®/TREMFYA One-Press® dose. TREMFYA®/TREMFYA One-Press® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

To monitor outcomes in women exposed to TREMFYA® during pregnancy, a pregnancy registry has been established. Healthcare professionals are encouraged to register patients and pregnant women are encouraged to enroll themselves by calling 1-877-311- 8972.

### 7.1.2 Breast-feeding

There are no data on the presence of guselkumab in human milk, the effects on the breastfed infant, or the effects on milk production. Guselkumab was not detected in the milk of lactating cynomolgus monkeys (see [16 NON-CLINICAL TOXICOLOGY](#)). The developmental and health



benefits of breastfeeding should be considered, as well as any potential adverse effects on the breastfed infant.

### 7.1.3 Pediatrics

The safety and efficacy of TREMFYA®/TREMFYA One-Press® in pediatric patients have not been evaluated.

### 7.1.4 Geriatrics

Of the 3406 plaque psoriasis and psoriatic arthritis patients exposed to TREMFYA®/TREMFYA One-Press® in Phase 2 and Phase 3 clinical trials, a limited number of patients were 65 years or older (n = 185, 5%) or 75 years and older (n=13, 0.4%). Thus data in these age groups are limited (see [10 CLINICAL PHARMACOLOGY](#)).

## 8 ADVERSE REACTIONS

### 8.1 Adverse Reaction Overview

The most frequently reported adverse drug reaction (>10%) through the placebo-controlled period of the phase 3 plaque psoriasis and psoriatic arthritis clinical trials in TREMFYA®-treated patients was respiratory tract infections.

In the placebo-controlled period of the phase 3 studies in plaque psoriasis, the proportion of TREMFYA®-treated patients who discontinued treatment due to adverse events was 1.3% (11/823) compared to 0.9% (8/422) in placebo- treated patients. Serious adverse events were reported in 1.9% (16/823) of TREMFYA®-treated patients and 1.4% (6/422) of placebo-treated patients through 16 weeks.

In the placebo-controlled period of the phase 3 studies in psoriatic arthritis, the proportion of TREMFYA®-treated patients who discontinued treatment due to adverse events was 1.7% (13/748) compared to 1.9% (7/372) in placebo- treated patients. Serious adverse events were reported in 2.0% (15/748) of TREMFYA®-treated patients and 3.2% (12/372) of placebo-treated patients through 24 weeks.

Overall, the safety profile was generally similar across indications.

### 8.2 Clinical Trial Adverse Reactions

*Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.*

The safety profile of TREMFYA®/TREMFYA One-Press® is based on data from the Phase 2 (PSO2001) and Phase 3 (VOYAGE 1, VOYAGE 2, NAVIGATE, and ORION) studies in plaque psoriasis and the Phase 2 (PSA2001) and the Phase 3 (DISCOVER 1 and DISCOVER 2) studies in psoriatic arthritis. Of the 3406 TREMFYA®- and TREMFYA One-Press®-treated patients, 2716 patients were exposed for at least 1 year, and 1917, 1482, 1393 and 950 patients were exposed for at least 2, 3, 4 and 5 years, respectively. Most patients (n=2516) received a

dosage regimen of 100 mg TREMFYA®/TREMFYA One-Press® as subcutaneous injection every 8 weeks. In the phase 3 psoriatic arthritis trials 725 patients (including placebo crossovers) received a dosage regimen of 100 mg TREMFYA® as subcutaneous injection every 4 weeks.

### Adverse Drug Reactions in Plaque Psoriasis Trials

Table 1 provides a summary of adverse reactions that occurred at a rate of at least 1% and at a higher rate in the TREMFYA® group than in the placebo group during the 16-week, placebo-controlled period of the pooled clinical trials, VOYAGE 1 and VOYAGE 2.

**Table 1: Adverse reactions reported by ≥1% of patients through Week 16 in VOYAGE 1 and VOYAGE 2**

	Placebo N = 422 n (%)	TREMFYA® <sup>a</sup> N = 823 n (%)	Adalimumab <sup>b</sup> N = 581 n (%)
<b>Gastrointestinal disorders</b>			
Diarrhea	4 (0.9%)	13 (1.6%)	7 (1.2%)
<b>General disorders and administration site conditions</b>			
Injection site reactions <sup>c</sup>	12 (2.8%)	37 (4.5%)	42 (7.2%)
<b>Infections and Infestations</b>			
Upper respiratory infections <sup>d</sup>	54 (12.8%)	118 (14.3%)	80 (13.8%)
Gastroenteritis <sup>e</sup>	4 (0.9%)	11 (1.3%)	8 (1.4%)
Herpes simplex infections <sup>f</sup>	2 (0.5%)	9 (1.1%)	8 (1.4%)
Tinea infections <sup>g</sup>	0	9 (1.1%)	3 (0.5%)
<b>Musculoskeletal and connective tissue disorders</b>			
Arthralgia	9 (2.1%)	22 (2.7%)	11 (1.9%)
<b>Nervous system disorders</b>			
Headache <sup>h</sup>	14 (3.3%)	38 (4.6%)	18 (3.1%)

<sup>a</sup> Subjects received 100 mg of TREMFYA® at Week 0, Week 4, and every 8 weeks thereafter;

<sup>b</sup> Subjects received adalimumab at 80 mg Week 0, 40 mg week 1 then 40 mg q2w thereafter

<sup>c</sup> Injection site reactions include injection site erythema, bruising, hematoma, hemorrhage, swelling, edema, pruritus, pain, discoloration, induration, inflammation, and urticaria.

<sup>d</sup> Upper respiratory infections include nasopharyngitis, upper respiratory tract infection (URTI), pharyngitis, and viral URTI.

<sup>e</sup> Gastroenteritis includes gastroenteritis and viral gastroenteritis

<sup>f</sup> Herpes simplex infections include oral herpes, herpes simplex, genital herpes, genital herpes simplex, and nasal herpes simplex.

<sup>g</sup> Tinea infections include tinea pedis, tinea cruris, tinea infection, and tinea manuum infections.

<sup>h</sup> Headache includes headache and tension headache.

## **Safety profile through Week 264 in Plaque Psoriasis Trials**

Through week 48 of VOYAGE 1 and VOYAGE 2, the types and the frequency of the adverse reactions in the TREMFYA®-treated patients were similar to those observed during the first 16 weeks of treatment.

Among 1221 patients who were initially randomized to TREMFYA® or who crossed over from placebo, 1119 patients received open-label TREMFYA® in the uncontrolled extension periods of VOYAGE 1 and VOYAGE 2. Through up to 5 years (N=1221; median duration of follow-up of 262.1 weeks [Range: 1-276]), the safety profile of TREMFYA® was consistent with that observed in the controlled periods of VOYAGE 1 and VOYAGE 2.

### **Adverse Drug Reactions in Psoriatic Arthritis Trials**

Table 2 provides a summary of adverse reactions that occurred at a rate of at least 1% and at a higher rate in the TREMFYA® group than in the placebo group during the 24-week, placebo-controlled period of the pooled clinical trials, DISCOVER 1 and DISCOVER 2.

**Table 2: Adverse reactions reported by ≥1% of patients through Week 24 in DISCOVER 1 and DISCOVER 2**

	Placebo N = 372 n (%)	TREMFYA® q8w <sup>a</sup> N = 375 n (%)	TREMFYA® q4w <sup>b</sup> N = 373 n (%)
<b>Gastrointestinal disorders</b>			
Diarrhea	3 (0.8%)	6 (1.6%)	4 (1.1%)
<b>General disorders and administration site conditions</b>			
Injection site reactions <sup>c</sup>	1 (0.3%)	5 (1.3%)	3 (0.8%)
<b>Infections and Infestations</b>			
Respiratory tract infections <sup>d</sup>	45 (12.1%)	46 (12.3%)	52 (13.9%)
<b>Investigations</b>			
Transaminases increased <sup>e</sup>	17 (4.6%)	31 (8.3%)	32 (8.6%)
Neutrophil count decreased <sup>f</sup>	3 (0.8%)	7 (1.9%)	7 (1.9%)
<b>Nervous system disorders</b>			
Headache <sup>g</sup>	3 (0.8%)	8 (2.1%)	7 (1.9%)

<sup>a</sup> Patients received 100 mg of TREMFYA® at Week 0, Week 4, and every 8 weeks thereafter

<sup>b</sup> Patients received 100 mg of TREMFYA® at Week 0, Week 4, and every 4 weeks thereafter

<sup>c</sup> Injection site reactions include injection site erythema, bruising, hematoma, hemorrhage, swelling, edema, pruritus, pain, discoloration, induration, inflammation, and urticaria.

<sup>d</sup> Respiratory tract infections include nasopharyngitis, upper respiratory tract infection (URTI), bronchitis, pharyngitis, and viral URTI.

<sup>e</sup> Transaminases increased includes alanine aminotransferase increased, aspartate aminotransferase increased, hepatic enzyme increased, transaminases increased, liver function test abnormal, hypertransaminasaemia

<sup>f</sup> Neutrophil count decreased includes neutrophil count decreased and neutropenia

<sup>g</sup> Headache includes headache and tension headache.

Among the 1120 adult patients with active psoriatic arthritis from DISCOVER 1 and DISCOVER 2, who were initially randomized to TREMFYA® or placebo, 1074 patients (including those who crossed over from placebo) received TREMFYA® at or after week 24 in the double-blind, not placebo-controlled, active treatment periods of DISCOVER 1 and DISCOVER 2. Through 1 year in DISCOVER 1 and 2 years in DISCOVER 2, the safety profile of TREMFYA® was consistent with that observed in the controlled periods.

### **Infections**

Infections have been observed in clinical trials in plaque psoriasis (23% for TREMFYA® vs 21% for placebo; ≤ 0.2% serious infections in both groups) and psoriatic arthritis (21% in both TREMFYA® and placebo groups; ≤ 0.8% serious infections in both groups).

In plaque psoriasis or psoriatic arthritis trials, adverse events of infection reported in ≥ 1% of patients treated with TREMFYA® through the placebo-controlled period were respiratory tract infections, gastroenteritis, tinea infections, and herpes simplex infections.

### **Immunogenicity**

As with all therapeutic proteins, there is the potential for immunogenicity with TREMFYA®. The immunogenicity of TREMFYA® was evaluated using a sensitive and drug-tolerant immunoassay. In subjects with psoriasis in clinical trials (PSO2001, VOYAGE 1, VOYAGE 2, and NAVIGATE), approximately 6% of patients treated with TREMFYA® developed antidrug antibodies in up to 52 weeks of treatment. Of the patients who developed antidrug antibodies, approximately 7% had antibodies that were classified as neutralizing which equates to 0.4% of all patients treated with TREMFYA®. Among the 46 subjects who developed antibodies to guselkumab and had evaluable data, 21 subjects exhibited lower trough levels of guselkumab, including one subject who experienced loss of efficacy after developing high antibody titers. However, antibodies to guselkumab were generally not associated with changes in clinical response or development of injection-site reactions.

In patients with psoriatic arthritis in clinical trials, 2% (n=15) of patients treated with TREMFYA® developed antidrug antibodies in up to 24 weeks of treatment. Of these patients, 1 (7%) had antibodies that were classified as neutralizing which equates to 0.1% of all psoriatic arthritis patients treated with TREMFYA®. None developed injection site reactions through Week 24. Overall, the small number of patients who were positive for antibodies to guselkumab limits definitive conclusion of the effect of immunogenicity on the pharmacokinetics, safety, and efficacy of guselkumab.

The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of incidence of antibodies to TREMFYA® with the incidences of antibodies to other products may be misleading.

### **Elevated Liver Enzymes**

During the placebo-controlled period of the plaque psoriasis clinical trials, adverse events of increases in liver enzymes were reported in 2.6% of TREMFYA® treated patients and 1.9% of placebo-treated patients. None of these events led to discontinuation of TREMFYA® treatment.

During the placebo-controlled period of the two phase 3 psoriatic arthritis clinical trials, adverse events of transaminases increased (includes alanine aminotransferase (ALT) increased, aspartate aminotransferase (AST) increased, hepatic enzyme increased, transaminases increased, liver function test abnormal, and hypertransaminasaemia) were reported more frequently in the TREMFYA®-treated patients (8.3% of q8w group, and 8.6% of q4w group) than in the placebo-treated patients (4.6%).

Based on laboratory assessments, an increased incidence of liver enzyme elevations was observed in patients treated with TREMFYA® q4w compared to patients treated with TREMFYA® q8w or placebo. Most transaminase increases (ALT and AST) were ≤ 3 x upper limit of normal (ULN). Transaminase increases from > 3 to ≤ 5 x ULN and > 5 x ULN were low in frequency (Table 3). A similar pattern was observed through the end of the 2-year Phase 3 psoriatic arthritis clinical study (DISCOVER 2). In most cases, the increase in transaminases was transient and did not lead to discontinuation of treatment.

**Table 3: Frequency of patients with transaminase increases post-baseline in two Phase III psoriatic arthritis clinical studies**

	Through Week 24 <sup>a</sup>			Through 1 Year <sup>b</sup>	
	Placebo N=370 <sup>d</sup>	TREMFYA® 100 mg q8w N=373 <sup>d</sup>	TREMFYA® 100 mg q4w <sup>c</sup> N=371 <sup>d</sup>	TREMFYA® 100 mg q8w N=373 <sup>d</sup>	TREMFYA® 100 mg q4w <sup>c</sup> N=371 <sup>d</sup>
<b>ALT</b>					
>1 to ≤3 x ULN	30.0%	28.2%	35.0%	33.5%	41.2%
>3 to ≤ 5 x ULN	1.4%	1.1%	2.7%	1.6%	4.6%
>5 x ULN	0.8%	0.8%	1.1%	1.1%	1.1%
<b>AST</b>					
>1 to ≤3 x ULN	20.0%	18.8%	21.6%	22.8%	27.8%
>3 to ≤ 5 x ULN	0.5%	1.6%	1.6%	2.9%	3.8%
>5 x ULN	1.1%	0.5%	1.6%	0.5%	1.6%

<sup>a</sup> placebo-controlled period

<sup>b</sup> patients randomized to placebo at baseline and crossed over to TREMFYA® are not included

<sup>c</sup> q4w dosing is not recommended in psoriatic arthritis patients

<sup>d</sup> number of patients with at least one post-baseline assessment for the specific laboratory test within the time period

### 8.3 Less Common Clinical Trial Adverse Reactions

Adverse reactions that occurred at rates <1% in the TREMFYA® group during the placebo controlled- period of the pooled plaque psoriasis and psoriatic arthritis clinical trials.

**Infections and Infestations:** candida infections, gastroenteritis, herpes simplex infections, tinea infections

**Nervous system disorders:** migraine

**Skin and subcutaneous tissue disorders:** urticaria

### 8.5 Post-Market Adverse Reactions

The following adverse reactions have been reported during post-marketing experience. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency reliably or establish a causal relationship to drug exposure.

**Immune System disorders:** anaphylaxis, hypersensitivity  
**Skin and Subcutaneous Tissue Disorders:** rash, urticaria

## 9 DRUG INTERACTIONS

### 9.4 Drug-Drug Interactions

#### Live vaccines

Live vaccines should not be given while a patient is undergoing therapy with TREMFYA®/TREMFYA One-Press® (see [7 WARNINGS AND PRECAUTIONS](#), Immune).

#### Immunosuppression Therapy

The safety and efficacy of TREMFYA®/TREMFYA One-Press® in combination with immunosuppressant drugs, including biologics, or with phototherapy, have not been evaluated.

#### Interactions with CYP450 Substrates

The formation of cytochrome P450 (CYP) enzymes can be altered by increased levels of certain cytokines (e.g., interleukin [IL]-1 $\beta$ , IL-6, tumor necrosis factor-alpha, and interferon) during chronic inflammation.

In a Phase 1 drug-drug interaction study in subjects (N=12) with moderate to severe plaque psoriasis, the results suggested a low potential for clinically relevant drug interactions between a single SC dose of guselkumab and substrates metabolized by CYP3A4, CYP2C9, CYP2C19, and CYP1A2. However, the results were highly variable and the interaction potential of guselkumab with drugs metabolized by CYP2D6 cannot be ruled out.

Upon initiation of TREMFYA® in patients who are receiving concomitant CYP450 substrates, particularly those with a narrow therapeutic index, consider monitoring for therapeutic effect or drug concentration and consider dosage adjustment as needed.

### 9.5 Drug-Food Interactions

Interactions with food have not been established.

### 9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

### 9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

## 10 CLINICAL PHARMACOLOGY

### 10.1 Mechanism of Action

Guselkumab is a human IgG1 $\lambda$  monoclonal antibody (mAb) that binds selectively to the p19 subunit of interleukin 23 (IL-23) and inhibits its interaction with cell surface IL-23 receptor. IL-23 is a naturally-occurring cytokine that is involved in normal inflammatory and immune responses. Guselkumab inhibits the release of proinflammatory cytokines and chemokines (e.g. IL-17A, IL-

17F and IL-22). Levels of IL-23 are elevated in the skin of patients with plaque psoriasis.

## 10.2 Pharmacodynamics

In clinical trials in patients with plaque psoriasis, guselkumab reduced serum levels of IL-17A, IL-17F and IL-22 relative to pre-treatment levels based on exploratory analyses of these pharmacodynamic markers.

In Phase 3 studies in psoriatic arthritis, evaluated patients had elevated serum levels of the acute phase proteins C-reactive protein, serum amyloid A and IL-6, and the Th17 effector cytokines IL-17A, IL-17F and IL-22 at baseline. Exploratory analyses found serum levels of these proteins measured at Week 4 and Week 24 were decreased compared to baseline following guselkumab treatment.

The relationship between these pharmacodynamic markers and the mechanism(s) by which guselkumab exerts its clinical effects is unknown.

## 10.3 Pharmacokinetics

Guselkumab exhibited linear pharmacokinetics in healthy subjects or patients with psoriasis over a dose range from 10 mg to 300 mg following subcutaneous injections.

The pharmacokinetics of guselkumab in subjects with psoriatic arthritis was similar to that in subjects with plaque psoriasis.

### Absorption:

Following a single 100 mg subcutaneous injection in healthy subjects, guselkumab reached a mean ( $\pm$  SD) maximum serum concentration ( $C_{max}$ ) of  $8.09 \pm 3.68$  mcg/mL by approximately 5.5 days post dose.

In subjects with psoriasis, steady-state serum guselkumab concentrations were achieved by Week 20 following subcutaneous administrations of 100 mg guselkumab at Weeks 0 and 4, and every 8 weeks thereafter. The mean ( $\pm$  SD) steady-state trough serum guselkumab concentrations in two Phase 3 studies were  $1.15 \pm 0.73$  mcg/mL and  $1.23 \pm 0.84$  mcg/mL.

In subjects with psoriatic arthritis, following subcutaneous administration of 100 mg of TREMFYA<sup>®</sup> at Weeks 0, 4, and every 8 weeks thereafter, mean ( $\pm$  SD) steady-state trough serum guselkumab concentration was approximately  $1.18 \pm 0.87$  mcg/mL.

The absolute bioavailability of guselkumab following a single 100 mg subcutaneous injection was estimated to be approximately 49% in healthy subjects.

### Distribution:

In subjects with plaque psoriasis, apparent volume of distribution was 13.5 L.

### Metabolism:

The exact pathway through which guselkumab is metabolized has not been characterized. As a human IgG monoclonal antibody, guselkumab is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG.

## Elimination:

Apparent clearance in subjects with plaque psoriasis was 0.516 L/day. Mean half-life ( $T_{1/2}$ ) of guselkumab was approximately 17 days in healthy subjects and approximately 15 to 18 days in subjects with plaque psoriasis across studies.

Clearance and volume of distribution of guselkumab increase as body weight increases, based on population pharmacokinetic analyses. However, observed clinical trial data indicate that dose adjustment for body weight is not warranted.

Population pharmacokinetic analyses indicated that concomitant use of acetaminophen, NSAIDs, oral corticosteroids and conventional DMARDs such as methotrexate, did not affect the clearance of guselkumab.

## Special Populations and Conditions

- **Pediatrics:** The safety and efficacy of guselkumab have not been established in pediatric patients.
- **Geriatrics:** Of the 1384 plaque psoriasis patients exposed to TREMFYA® in phase 3 clinical studies and included in the population pharmacokinetic analysis (pop PK), 70 subjects were 65 years of age or older, including 4 subjects who were 75 years of age or older. Population pharmacokinetic analyses indicated there were no apparent changes in clearance estimate in subjects  $\geq 65$  years of age compared to subjects  $< 65$  years of age, suggesting no dose adjustment is needed for elderly patients. Of the 746 psoriatic arthritis patients exposed to TREMFYA® in phase III clinical studies and included in the pop PK analysis, a total of 38 patients were 65 years of age or older, and no patients were 75 years of age or older.
- **Gender, Race, Age:** The clearance of guselkumab was not impacted by sex, age, or race.
- **Hepatic Insufficiency:** No specific study has been conducted to determine the effect of hepatic impairment on the pharmacokinetics of guselkumab.
- **Renal Insufficiency:** No specific study has been conducted to determine the effect of renal impairment on the pharmacokinetics of guselkumab.

## 11 STORAGE, STABILITY AND DISPOSAL

TREMFYA®/TREMFYA One-Press® is sterile and preservative-free. Discard any unused portion after injection.

Store in a refrigerator at 2°C to 8°C (36°F to 46°F). Do not freeze.

Store in original carton until time of use. Protect from light. Do not shake.

Keep out of sight and reach of children.

## 12 SPECIAL HANDLING INSTRUCTIONS

Following administration of TREMFYA®/TREMFYA One-Press®, discard any unused portion. The product should be disposed of in a puncture resistant container. Patients or caregivers should be instructed on how to properly dispose of the product, and told not to reuse these items.



## PART II: SCIENTIFIC INFORMATION

### 13 PHARMACEUTICAL INFORMATION

#### Drug Substance

Proper name: guselkumab

Chemical name: guselkumab

Molecular formula and molecular mass: Guselkumab is a fully human immunoglobulin IgG1 $\lambda$  mAb with an average molecular weight of 146,613 Daltons

Physicochemical properties: TREMFYA®/TREMFYA One-Press® (guselkumab injection) is a clear and colorless to light yellow solution and essentially free of visible particulate material with a pH of approximately 5.8

#### Product Characteristics:

TREMFYA® is supplied as a 100 mg/mL sterile solution in a single-dose 1 mL glass syringe with a fixed 27G, half inch needle assembled in a passive needle guard delivery system.

TREMFYA One-Press® is supplied as a 100 mg/mL sterile solution in a single-dose 1 mL glass syringe with a fixed 27G, half inch needle assembled in a patient-controlled injector.

TREMFYA®/TREMFYA One-Press® does not contain preservatives.

### 14 CLINICAL TRIALS

#### 14.1 Clinical Trials by Indication

##### Plaque Psoriasis

Table 4: Summary of trial designs and patient demographics

Study #	Trial design	Dosage, route of administration and duration	Total number of subjects	Mean age (Range)	Gender
VOYAGE 1	A phase 3, multicenter, randomized, double-blind, placebo and active comparator controlled study	Guselkumab (n=329) 100 mg SC Weeks 0, 4 then q8w Placebo (n=174) SC Weeks 0, 4, 12 → guselkumab 100 mg SC Week 16, 20 then q8w <sup>a</sup> Adalimumab (n=334) SC 80 mg Week 0, 40 mg week 1 then 40 mg q2w. <sup>b</sup>	837	43.7 (18-87)	M=608 F=229

VOYAGE 2	A phase 3, multicenter, randomized, double-blind, placebo and active comparator controlled study	Guselkumab (n=496) 100 mg SC Weeks 0, 4, 12 and 20 <sup>c</sup> Placebo (n=248) SC Weeks 0, 4, 12 → guselkumab 100 mg SC Week 16, 20 <sup>a</sup> Adalimumab (n=248) 80 mg Week 0, 40 mg week 1 then 40 mg q2w. <sup>d</sup>	992	43.0 (18-74)	M=692 F=300
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<sup>a</sup> The placebo group crossed over to receive guselkumab at Weeks 16 and 20 then q8w

<sup>b</sup> All subjects, including those randomized to adalimumab at Week 0, received TREMFYA® 100 mg at Week 52 and every 8 weeks thereafter.

<sup>c</sup> Subjects randomized to TREMFYA® at Week 0 who were PASI 90 responders at Week 28 were re-randomized to either continue treatment with TREMFYA® maintenance therapy or withdrawal of therapy.

<sup>d</sup> PASI 90 non-responders at week 28 started to receive TREMFYA® at week 28 and then week 32 and every 8 weeks thereafter.

The efficacy and safety of TREMFYA® was assessed in two Phase 3, multicenter, randomized, double-blind studies (VOYAGE 1 and VOYAGE 2) in patients 18 years or older with moderate to severe plaque psoriasis (with or without psoriatic arthritis) defined by Investigator's Global Assessment (IGA)  $\geq 3$ , a Body Surface Area (BSA) involvement  $\geq 10\%$ , and Psoriasis Area and Severity Index (PASI) score  $\geq 12$ , and were candidates for systemic therapy or phototherapy for psoriasis. Patients with guttate, erythrodermic, or pustular psoriasis were excluded from the studies. No concomitant antipsoriatic therapies were allowed during the studies.

The two pivotal studies (VOYAGE 1 and 2) evaluated the efficacy and safety of guselkumab for the treatment of subjects with moderate to severe plaque-type psoriasis and enrolled a total of 1829 patients who were randomized to placebo, TREMFYA®, or adalimumab.

The co-primary endpoints in VOYAGE 1 and VOYAGE 2 were the proportions of patients who achieved an IGA score of cleared (0) or minimal (1) and the proportions of patients who achieved a PASI 90 response at Week 16, comparing the TREMFYA® group and the placebo group.

The IGA is a 5-category scale: 0 = cleared, 1 = minimal, 2 = mild, 3 = moderate, 4 = severe, that indicates the physician's overall assessment of psoriasis focusing on plaque thickness/induration, erythema and scaling.

Other endpoints included the proportions of patients who achieved an IGA score of cleared (0), a PASI 100, PASI 75 response and regional disease as measured by scalp-specific IGA (ss-IGA). Patient-reported outcomes were assessed based on the Psoriasis Symptoms and Signs Diary (PSSD) and Dermatology Life Quality Index (DLQI).

Baseline disease characteristics were generally consistent across all treatment groups for the study populations in VOYAGE 1 and 2 with a median BSA of 22% and 24%, a median baseline PASI score of 19 for both studies, a baseline IGA score of severe for 25% and 23% of patients, and a history of psoriatic arthritis for 19% and 18% patient, respectively.

Of all patients who were included in the VOYAGE 1 and VOYAGE 2 studies, 32% and 29% were naïve to conventional systemic and biologic systemic therapy; 54% and 57% had received prior phototherapy, and 62% and 64% had received prior conventional systemic therapy, respectively. In both studies, 21% had received prior biologic systemic therapy, including 11% who had received at least one anti-tumour necrosis factor alpha (TNF $\alpha$ ) agent, and approximately 10% who had received an anti-IL-12/IL-23 agent.

The results of VOYAGE 1 and VOYAGE 2 studies are presented in Table 5 and Table 6 below.

**Table 5: Summary of Clinical Responses at Week 16 (NRI<sup>a</sup>) in Psoriasis Studies (Co-Primary Endpoints)**

	VOYAGE 1			VOYAGE 2		
	TREMFYA <sup>®</sup> (N=329) n (%)	Placebo (N=174) n (%)	Treatment difference <sup>b</sup> (95% CI)	TREMFYA <sup>®</sup> (N=496) n (%)	Placebo (N=248) n (%)	Treatment difference <sup>b</sup> (95% CI)
<b>IGA response of 0/1</b>	280 (85%) <sup>c</sup>	12 (7%)	78% (73%,83%)	417 (84%) <sup>c</sup>	21 (8%)	76% (71%,80%)
<b>PASI 90 response</b>	241 (73%) <sup>c</sup>	5 (3%)	70% (65%,76%)	347 (70%) <sup>c</sup>	6 (2%)	68% (64%,72%)

<sup>a</sup> Non-responder imputation.

<sup>b</sup> Treatment difference versus placebo adjusted by investigator site with Mantel-Haenszel weights.

<sup>c</sup> p-value < 0.001; p-value is based on the Cochran-Mantel-Haenszel chi-square test stratified by investigator site.

**Table 6: Summary of Clinical Responses (NRI<sup>a</sup>) in Psoriasis Studies (Secondary Endpoints)**

	VOYAGE 1			VOYAGE 2		
	TREMFYA <sup>®</sup> (N=329) n (%)	Adalimumab (N=334) n (%)	Treatment difference <sup>b</sup> (95% CI)	TREMFYA <sup>®</sup> (N=496) n (%)	Adalimumab (N=248) n (%)	Treatment difference <sup>b</sup> (95% CI)
<b>IGA response of 0/1</b>						
Week 16	280 (85%) <sup>c</sup>	220 (66%)	19% (13%,25%)	417 (84%) <sup>c</sup>	168 (68%)	16% (11%,22%)
Week 24	277 (84%) <sup>c</sup>	206 (62%)	23% (17%,29%)	414 (83%) <sup>c</sup>	161 (65%)	18% (12%,25%)
<b>IGA response of 0</b>						
Week 24	173 (53%) <sup>c</sup>	98 (29%)	25% (18%,31%)	257 (52%) <sup>c</sup>	78 (31%)	20% (13%,27%)
<b>PASI 75 response</b>						
Week 16	300 (91%) <sup>c</sup>	244 (73%)	18% (13%,23%)	428 (86%) <sup>c</sup>	170 (69%)	18% (12%,24%)
<b>PASI 90 response</b>						
Week 16	241 (73%) <sup>c</sup>	166 (50%)	24% (17%,31%)	347 (70%) <sup>c</sup>	116 (47%)	23% (17%,30%)
Week 24	264 (80%) <sup>c</sup>	177 (53%)	28% (22%,34%)	373 (75%) <sup>c</sup>	136 (55%)	20% (14%,27%)

<sup>a</sup> Non-Responder Imputation.

<sup>b</sup> Treatment difference versus adalimumab adjusted by investigator site with Mantel-Haenszel weights.

<sup>c</sup> p-value < 0.001; p-value is based on the Cochran-Mantel-Haenszel chi-square test stratified by investigator site. Type 1 error rate is controlled based on a pre-defined hierarchical testing procedure.

TREMFYA<sup>®</sup> demonstrated superiority to placebo for the co-primary endpoints of IGA cleared (0) or minimal (1), and PASI 90 at week 16 (Table 5).

In addition, TREMFYA<sup>®</sup> demonstrated statistical superiority to adalimumab for IGA cleared or minimal (0 or 1), PASI 90 and PASI 75 at week 16 and IGA cleared (0), IGA cleared or minimal (0 or 1) and PASI 90 at week 24 (see Table 6). In VOYAGE 1, with continued treatment over 48 weeks, IGA cleared (0), IGA cleared or minimal (0 or 1) and PASI 90 responses in guselkumab treated patients were maintained and remained significantly greater than those achieved with adalimumab (IGA cleared (0), 50% vs 26%, IGA cleared or minimal (0 or 1), 81% vs 55%, PASI 90, 76% vs. 48%).

In the VOYAGE 1 study, at week 16, 37% of patients receiving TREMFYA<sup>®</sup> achieved PASI 100 compared to 17% of adalimumab treated patients, and 1% of placebo treated patients. In VOYAGE 2, at Week 16, 34% of patients receiving TREMFYA<sup>®</sup> achieved PASI 100 compared to 21% of adalimumab treated patients, and 1% of placebo-treated patients.

In VOYAGE 1, among 494 patients randomized to TREMFYA<sup>®</sup> or who crossed over from placebo, 460 patients received open-label TREMFYA<sup>®</sup> in the uncontrolled extension period after week 48. At week 252, 76.9% (380/494) of patients remained on TREMFYA<sup>®</sup> and 66.6% (329/494) achieved PASI 90.

In TREMFYA<sup>®</sup> treated-patients, improvement was seen in psoriasis involving the scalp (as measured by the Scalp-specific Investigator Global Assessment [ss-IGA]). Specifically, in the subset of patients with a baseline ss-IGA score  $\geq 2$ , 83.4% and 80.6% in the TREMFYA<sup>®</sup> group in VOYAGE 1 and VOYAGE 2, respectively, achieved an ss-IGA score of 0 or 1 and at least a 2-grade improvement from baseline compared to 14.5% and 10.9% in the placebo group, respectively at week 16.

### **Maintenance and Durability of Response**

To evaluate the maintenance and durability of response, patients originally randomized to TREMFYA<sup>®</sup> and who were PASI 90 responders at Week 28 in the VOYAGE 2 study were re-randomized to continue maintenance treatment with TREMFYA<sup>®</sup> or be withdrawn from therapy (i.e., placebo). At week 48, 88.6% of patients in the continuous maintenance treatment group were PASI 90 responders compared with 36.8% in the withdrawal group. By week 72, 86.0% of patients in the continuous maintenance treatment group were PASI 90 responders compared with 11.5% in the withdrawal group.

### **Patient-reported Outcomes**

Significantly greater improvements in psoriasis symptoms (itch, pain, stinging, burning and skin tightness) at Week 16 were seen in TREMFYA<sup>®</sup> compared to placebo in both studies based on the Psoriasis Symptoms and Signs Diary (PSSD). Significantly greater proportions of patients on TREMFYA<sup>®</sup> compared to adalimumab achieved a PSSD symptom score of 0 (symptom-free) at Week 24 in both studies.

Improvements in the Dermatology Life Quality Index (DLQI) from baseline were observed in

patients treated with TREMFYA® compared to placebo at Week 16.

### Active-Controlled Study in Ustekinumab Inadequate Responders – NAVIGATE

The NAVIGATE study evaluated the efficacy of 24 weeks of treatment with TREMFYA® in patients (N=268) who had an inadequate response (defined as IGA  $\geq 2$ ) at Week 16 after initial treatment with ustekinumab (dosed at Week 0 and Week 4). These patients were randomized to either continue ustekinumab treatment every 12 weeks or to switch to TREMFYA® 100 mg given at Weeks 16, 20, and every 8 weeks thereafter. Baseline characteristics for randomized subjects were similar to those observed in VOYAGE 1 and VOYAGE 2.

In patients with an inadequate response to ustekinumab, a greater proportion of patients who switched to TREMFYA® treatment achieved an IGA score of 0 or 1 and had a  $\geq 2$ -grade improvement at Week 28 compared to patients who continued ustekinumab treatment (31% vs 14%, respectively).

### TREMFYA One-Press® - ORION

ORION evaluated the efficacy, safety, and PK of guselkumab administered with the patient-controlled One-Press injector. In this study, 78 subjects were randomized to receive either TREMFYA One-Press® (100 mg at Weeks 0 and 4 and every 8 weeks thereafter, N= 62), or placebo (N= 16). Baseline characteristics for randomized subjects were comparable to those observed in VOYAGE 1 and VOYAGE 2. The co-primary endpoints were the same as those for VOYAGE 1 and VOYAGE 2. The secondary endpoints included the proportion of subjects who achieved an IGA score 0 at Week 16 and the proportion of subjects who achieved a PASI 100 response at Week 16.

A greater proportion of subjects in the guselkumab group achieved an IGA score of 0 or 1 or a PASI 90 response at Week 16 (81% and 76%, respectively) than in the placebo group (0% for both endpoints). The proportion of subjects who achieved an IGA score of 0 at Week 16 was higher in the guselkumab group compared to the placebo group (56.5% vs. 0%). The proportion of subjects who achieved a PASI 100 response at Week 16 was higher in the guselkumab group compared to the placebo group (50.0% vs. 0%).

## Psoriatic Arthritis

**Table 7: Summary of trial designs and patient demographics**

Study #	Trial design	Dosage, route of administration and duration	Total number of subjects	Mean age (Range)	Gender
DISCOVER 1	A phase 3, multicenter, randomized, double-blind, placebo-controlled study	Guselkumab (n=127) 100 mg SC Weeks 0, 4 then q8w Guselkumab (n=128) 100 mg SC Weeks 0, then q4w Placebo (n=126) SC Weeks 0, then q4w to Week 20 → guselkumab 100 mg SC Week 24, then q4w	381	48.4 (19-74)	M=195 F=186

DISCOVER 2	A phase 3, multicenter, randomized, double-blind, placebo-controlled study	Guselkumab (n=248) 100 mg SC Weeks 0, 4 then q8w Guselkumab (n=245) 100 mg SC Weeks 0, then q4w Placebo (n=246) SC Weeks 0, then q4w to Week 20 → guselkumab 100 mg SC Week 24, then q4w	739	45.7 (19-75)	M=388 F=351
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The safety and efficacy of TREMFYA® were assessed in 1120 patients in 2 randomized, double-blind, placebo-controlled studies (DISCOVER 1 and DISCOVER 2) in adult patients with active psoriatic arthritis (≥3 swollen joints, ≥3 tender joints, and a C-reactive protein (CRP) level of ≥0.3 mg/dL in DISCOVER 1 and ≥5 swollen joints, ≥5 tender joints, and a CRP level of ≥0.6 mg/dL in DISCOVER 2) who had inadequate response to standard therapies (e.g. conventional DMARDs [cDMARDs]), apremilast, or nonsteroidal anti-inflammatory drugs [NSAIDs]). Patients in these studies had a diagnosis of psoriatic arthritis for at least 6 months based on the Classification criteria for Psoriatic Arthritis (CASPAR) and a median duration of psoriatic arthritis of 4 years at baseline.

In DISCOVER 1 approximately 30% of patients had been previously treated with up to 2 anti-tumor necrosis factor alpha (anti-TNFα) agents whereas in DISCOVER 2 all patients were biologic naïve. Approximately 58% of patients from both studies had concomitant methotrexate (MTX) use. Patients with different subtypes of psoriatic arthritis were enrolled in both studies, including polyarticular arthritis with the absence of rheumatoid nodules (40%), spondylitis with peripheral arthritis (30%), asymmetric peripheral arthritis (23%), distal interphalangeal involvement (7%) and arthritis mutilans (1%). At baseline, over 65% and 42% of the patients had enthesitis and dactylitis, respectively and over 75% had ≥3% body surface area (BSA) psoriasis skin involvement. The primary endpoint in both studies was the percentage of patients achieving an ACR20 response at Week 24.

### Signs and Symptoms

The ACR responses at Week 24 are presented in Table 8 below. Comparable response rates were observed regardless of prior anti-TNFα exposure in DISCOVER 1, and in both trials comparable response rates were observed regardless of concomitant cDMARD use or previous treatment with cDMARDs.

Figure 1 shows the proportion of patients with ACR 20 response, by visit, up to Week 24 in DISCOVER 2.

**Table 8: Percent of Patients with ACR Responses<sup>a,b</sup> at Week 24 in DISCOVER 1 and DISCOVER 2**

	DISCOVER 1			DISCOVER 2		
	Placebo (N=126)	TREMFYA <sup>®</sup> 100 mg q8w (N=127)	Difference from Placebo (95% CI) p-value	Placebo (N=246)	TREMFYA <sup>®</sup> 100 mg q8w (N=248)	Difference from Placebo (95% CI) p-value
<b>ACR 20 response</b>	22.2%	52.0%	29.8% (18.6, 41.1) <0.001 <sup>c</sup>	32.9%	64.1%	31.2% (22.9, 39.5) <0.001 <sup>d</sup>
<b>ACR 50 response</b>	8.7%	29.9%		14.2%	31.5%	
<b>ACR 70 response</b>	5.6%	11.8%		4.1%	18.5%	

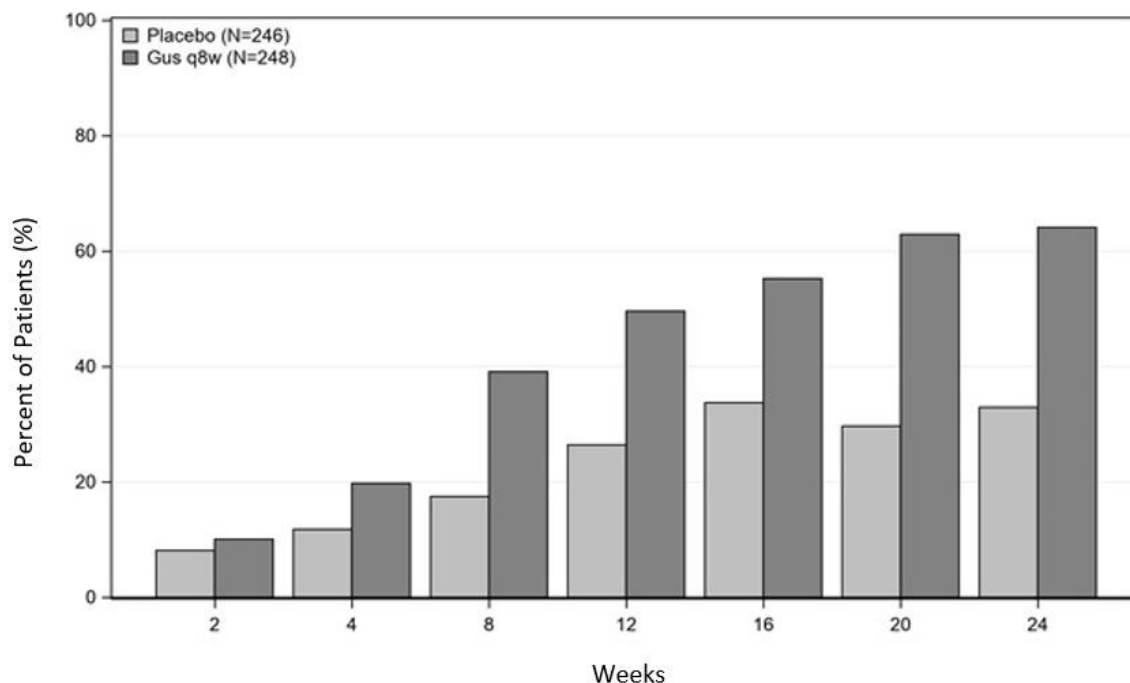
<sup>a</sup> Patients with <5% improvement from baseline in both tender and swollen joint counts at Week 16 were qualified for early escape and were permitted to initiate or increase the dose of concomitant medications including NSAIDs, oral corticosteroid and cDMARD, and remained on the randomized study treatment. At Week 16, 19.0% and 3.1% (DISCOVER 1) and 15.4% and 5.2%, (DISCOVER 2) of the patients in the placebo and TREMFYA<sup>®</sup> 100mg q8w groups respectively met early escape criteria.

<sup>b</sup> Patients with missing data at Week 24 were imputed as non-responders. Patients who initiated or increased the dose of cDMARD or oral corticosteroids over baseline, discontinued study or study medication, or initiated protocol prohibited medications/therapies for psoriatic arthritis prior to Week 24 were considered as treatment failures and non-responders. At Week 24, 16.7% and 5.5% (DISCOVER 1), and 6.9% and 4.8% (DISCOVER 2) of the patients in the placebo group and the TREMFYA<sup>®</sup> 100 mg q8w group met treatment failure criteria.

<sup>c</sup> Treatment differences, 95% CIs and p-values were based on the Cochran-Mantel-Haenszel test stratified by baseline non-biologic cDMARD and prior anti-TNF $\alpha$  agents.

<sup>d</sup> Treatment differences, 95% CIs and p-values were based on the Cochran-Mantel-Haenszel test stratified by baseline non-biologic cDMARD and prior CRP (<2.0,  $\geq$ 2.0 mg/dL).

**Figure 1: Percent of Patients Achieving ACR 20 Response by Visit Through Week 24 in DISCOVER 2**



In DISCOVER 1, among 127 patients randomized to TREMFYA® 100 mg q8w, 123 patients received TREMFYA® at or after 24 weeks in the double-blind, not placebo controlled, active treatment period. 91.3% (116/127) of patients remained on TREMFYA® at Week 48.

In DISCOVER 2, among 248 patients randomized to TREMFYA® 100 mg q8w, 240 patients received TREMFYA® at or after 24 weeks in the double-blind, not placebo controlled, active treatment period. 89.9% (223/248) of patients remained on TREMFYA® at Week 100.

In an exploratory analysis among TREMFYA® 100 mg q8w patients who achieved ACR 20 at Week 24, 80.6% (54/67) in DISCOVER 1 and 89.9% (143/159) in DISCOVER 2 were ACR 20 responders at Week 52; and 83% (132/159) were ACR 20 responders at Week 100 in DISCOVER 2.



**Table 9: Mean change from Baseline in ACR Component Scores at Week 24 Based on Observed Data**

	DISCOVER 1		DISCOVER 2	
	Placebo (N=126)	TREMFYA® 100 mg q8w (N=127)	Placebo (N=246)	TREMFYA® 100 mg q8w (N=248)
<b>No. of Swollen Joints</b>				
Baseline	10.1	10.9	12.3	11.7
Mean change at Week 24	-5.1	-7.3	-6.4	-8.1
<b>No. of Tender Joints</b>				
Baseline	19.8	20.2	21.6	19.8
Mean change at Week 24	-6.8	-10.5	-7.3	-10.4
<b>Patient's Assessment of Pain</b>				
Baseline	5.8	6.0	6.3	6.3
Mean change at Week 24	-0.7	-2.2	-1.1	-2.5
<b>Patient Global Assessment</b>				
Baseline	6.1	6.5	6.5	6.5
Mean change at Week 24	-0.9	-2.5	-1.2	-2.5
<b>Physician Global Assessment</b>				
Baseline	6.3	6.2	6.7	6.6
Mean change at Week 24	-2.2	-3.5	-2.5	-3.8
<b>Disability Index (HAQ-DI)</b>				
Baseline	1.2	1.2	1.3	1.3
Mean change at Week 24	-0.1	-0.3	-0.2	-0.4
<b>CRP (mg/dL)</b>				
Baseline	1.4	1.6	2.1	2.0
Mean change at Week 24	-0.0	-0.7	-0.5	-1.1

In DISCOVER 1, the proportion of patients who achieved Minimal Disease Activity (MDA) at Week 24 was 22.8% (29/127) in the TREMFYA® 100mg q8w group and 11.1% (14/126) in the placebo group. In DISCOVER 2, the proportion of patients who achieved MDA at Week 24 was 25% (62/248) in the TREMFYA® 100mg q8w group and 6.1% (15/246) in the placebo group.

**Psoriasis Skin Response**

In patients with ≥3% BSA psoriasis skin involvement and an IGA score of ≥2 at baseline, the proportion of patients who achieved a psoriasis response at Week 24, defined as an IGA of 0 (cleared) or 1 (minimal) and a ≥2-grade reduction from baseline, was assessed. In DISCOVER 1, the proportions of patients achieving a psoriasis IGA response were 57.3% and 15.4% for the TREMFYA® 100mg q8w and placebo dose groups respectively. In DISCOVER 2, the proportions of these patients achieving a psoriasis IGA response were 70.5% and 19.1% for the TREMFYA® 100mg q8w and placebo dose groups respectively.

### *Enthesitis and Dactylitis*

Treatment with TREMFYA® resulted in improvement in dactylitis and enthesitis in patients with pre-existing dactylitis or enthesitis at baseline.

### **Radiographic Response**

In DISCOVER 2, inhibition of structural damage progression was measured radiographically and expressed as the mean change from baseline in the total modified van der Heijde-Sharp (vdH-S) score at Week 24. The mean change (95% CI) in progression from baseline in the vdH-S was 0.52 (0.18, 0.96) for TREMFYA® 100 mg q8w and 0.95 (0.61, 1.29) for placebo at Week 24.

### **Physical Function and Other Patient Reported Outcomes**

At Week 24, a greater mean improvement from baseline in physical function, as measured by the Health Assessment Questionnaire-Disability Index (HAQ-DI) was shown in both studies in the TREMFYA® 100 mg q8w group compared to placebo. The mean change from baseline at Week 24 was -0.32 and -0.073 (DISCOVER 1) and -0.37 and -0.13 (DISCOVER 2) for the TREMFYA® 100mg q8w and placebo dose groups respectively (p<0.001 in both trials).

At Week 24, patients in the TREMFYA® group in both DISCOVER 1 and DISCOVER 2 showed greater improvement from baseline in the SF-36 PCS compared with placebo. At Week 24 there was numeric improvement in the physical functioning, role-physical, bodily-pain, general health, social-functioning and vitality domains but not in the role-emotional and mental health domains. Patients in the TREMFYA® group in both DISCOVER 1 and DISCOVER 2 showed improvement from baseline in fatigue measured with FACIT-fatigue at Week 24.

## **16 NON-CLINICAL TOXICOLOGY**

**General Toxicology:** In repeat-dose toxicity studies in cynomolgus monkeys, guselkumab was well-tolerated at weekly doses up to 50 mg/kg intravenously for 5 weeks or 50 mg/kg subcutaneously for up to 24 weeks. Additionally, there were no effects on cardiovascular, respiratory, and nervous system function, clinical pathology, or anatomical pathology parameters. At the NOAEL (50 mg/kg once weekly),  $C_{max}$  and  $AUC_{last}$  values were approximately 206-fold and 50-fold higher, respectively, than those following a single administration of a 100 mg SC dose to psoriasis patients (4.81 µg/mL and 108.48 µg•h/mL, respectively).

**Carcinogenicity and Genotoxicity:** Studies have not been conducted to evaluate the carcinogenic or genotoxic potential of guselkumab.

**Reproductive and Developmental Toxicology:** In a combined embryo-fetal developmental and pre- and post-natal development toxicity study, pregnant cynomolgus monkeys (19, 20, and 20 in the 0, 10 and 50 mg/kg groups, respectively) were administered weekly subcutaneous doses of guselkumab from the beginning of organogenesis to parturition. Neonatal deaths occurred in the offspring of 1 of 16 control monkeys and of 3 of 14 monkeys in each of the guselkumab-administered groups ( $C_{max}$  and  $AUC_{last}$  values were 31- and 8-fold greater, respectively, than the human levels). These neonatal deaths were attributed to maternal neglect, trauma, and early or late delivery, although a drug-related effect could not be ruled out.

Fetal losses (spontaneous abortions, including stillbirths) were also observed at all dose levels, all of which were within the historical control range for the testing facility, but for which a drug-related effect could also not be ruled out. The clinical significance of these findings is unknown. No guselkumab-related effects on functional or immunological development were observed in the infants from birth through 6 months of age.

No effects on fertility or early embryonic development were observed following administration of female guinea pigs with guselkumab at subcutaneous doses up to 100 mg/kg twice-weekly before mating, through mating, and during early gestation to implantation ( $C_{max}$  and  $AUC_{last}$  values were 106- and 12-fold greater, respectively, than the human levels).

In a male fertility and early embryonic development toxicity study conducted in guinea pigs, the incidence of total litter loss (5 of 22 untreated females) was increased following administration of males with guselkumab at a subcutaneous dose of 100 mg/kg twice weekly prior to mating and through mating for a total of 21 doses. In a second male fertility and early embryonic developmental toxicity study, there were no total litter losses in untreated females mated with treated males (100 mg/kg twice weekly). No effects on male fertility or early embryonic development were observed at a dose of 25 mg/kg ( $C_{max}$  and  $AUC_{last}$  values were 51- and 6-fold greater, respectively, than the human levels).

## PATIENT MEDICATION INFORMATION

### READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

**Pr**TREMFYA®  
**Pr**TREMFYA One-Press®  
(guselkumab injection)  
Solution for injection  
100 mg/ 1 mL

Read this carefully before you start taking **TREMFYA®/TREMFYA One-Press®** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **TREMFYA®/TREMFYA One-Press®**.

#### What is **TREMFYA®/TREMFYA One-Press®** used for?

- **Plaque Psoriasis**

**TREMFYA®/TREMFYA One-Press®** is a prescription medicine used to treat adults with moderate to severe “plaque psoriasis”, an inflammatory condition affecting the skin and nails. Plaque psoriasis can cause raised, thick, red and scaly patches (“psoriatic lesions”) that can appear anywhere on your body. **TREMFYA®/TREMFYA One-Press®** reduces the inflammation and other symptoms of the disease.

- **Psoriatic Arthritis**

**TREMFYA®/TREMFYA One-Press®** is used to treat adults with active psoriatic arthritis. Psoriatic arthritis is an inflammatory disease of the joints, usually accompanied by psoriasis. Psoriatic arthritis can cause pain, swelling and stiffness in the joints, in addition to a disruption in daily activities and fatigue. If you have active psoriatic arthritis, you will be given **TREMFYA®/TREMFYA One-Press®** alone or in combination with a conventional Disease Modifying Anti-Rheumatic Drug (cDMARD) such as methotrexate. **TREMFYA®/TREMFYA One-Press®** reduces signs and symptoms of your arthritis and may improve symptoms in patients that have psoriasis.

#### How does **TREMFYA®/TREMFYA One-Press®** work?

**TREMFYA®/TREMFYA One-Press®** contains the active substance guselkumab. Guselkumab is a monoclonal antibody. Monoclonal antibodies are proteins that recognize and bind specifically to certain proteins in the body. This medicine works by neutralizing the activity of a protein called IL-23, which is present at increased levels in diseases such as plaque psoriasis.

Using **TREMFYA®/TREMFYA One-Press®** should improve your skin clearance and reduce your symptoms of psoriasis such as itching, pain, stinging, burning and skin tightness. In addition, **TREMFYA®/TREMFYA One-Press®** helps reduce the signs and symptoms of psoriatic arthritis.

#### What are the ingredients in **TREMFYA®/TREMFYA One-Press®**?

Medicinal ingredients: guselkumab

Non-medicinal ingredients: L-histidine, L-histidine monohydrochloride monohydrate, polysorbate 80, sucrose and water for injection.

**TREMFYA® comes in the following dosage forms:**

100mg/mL solution for injection in a single-dose pre-filled syringe

**TREMFYA One-Press® comes in the following dosage forms:**

100mg/mL solution for injection in a single-dose patient-controlled injector

**Do not use TREMFYA®/TREMFYA One-Press® if:**

- You are allergic to guselkumab or any of the ingredients in TREMFYA®/TREMFYA One-Press®. See **What are the ingredients in TREMFYA®/TREMFYA One-Press®**.

If you think you are allergic, ask your healthcare professional for advice before using TREMFYA®/TREMFYA One-Press®.

**To help avoid side effects and ensure proper use, talk to your healthcare professional before you take TREMFYA®/TREMFYA One-Press®. Talk about any health conditions or problems you may have, including if you:**

- are being treated for an infection or if you have an infection that does not go away or keeps coming back. TREMFYA®/TREMFYA One-Press® may lower your ability to fight infections and may increase your risk of infections.
- have tuberculosis (TB) or have been in close contact with someone with TB.
- think you have an infection or have symptoms of an infection such as
  - fever or flu-like symptoms
  - muscle aches
  - cough
  - shortness of breath
  - burning when you urinate or urinating more often than normal
  - blood in your phlegm (mucus)
  - weight loss
  - warm, red or painful skin or sores on your body different from your psoriasis
  - diarrhea or stomach pain
- have recently had a vaccination or if you are due to have a vaccination during treatment with TREMFYA®/TREMFYA One-Press®. You should not be given certain types of vaccines (live vaccines) while using TREMFYA®/TREMFYA One-Press®.
- are pregnant, think that you may be pregnant or are planning to have baby. If you are a woman of childbearing potential, use adequate contraception while using TREMFYA®/TREMFYA One-Press® and for at least 12 weeks after the last TREMFYA®/TREMFYA One-Press® dose. Talk to your doctor about your contraception options.
- are breast-feeding or plan to breast-feed. You and your doctor should decide if you will breast-feed while using TREMFYA®/TREMFYA One-Press®.

**Look out for infections and allergic reactions**

- Do not use TREMFYA®/TREMFYA One-Press® if you have any symptoms of infection unless you are instructed by your healthcare provider.

- **After starting TREMFYA®/TREMFYA One-Press®, call your healthcare provider right away, if you have any of the symptoms of an infection listed above.**
- **Serious allergic reactions, which can include symptoms of a swollen face, lips, mouth, tongue or throat, difficulty swallowing or breathing, hives and shortness of breath, have occurred with TREMFYA®/TREMFYA One-Press®. Tell your doctor or seek medical help immediately if you experience these symptoms.**

#### **Children and adolescents (below the age of 18 years)**

TREMFYA®/TREMFYA One-Press® is not recommended for children and adolescents (under 18 years of age) because it has not been studied in this age group.

**Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.**

#### **How to take TREMFYA®/TREMFYA One-Press®:**

Always use this medicine exactly as your healthcare professional has told you. Check with your healthcare professional if you are not sure.

TREMFYA®/TREMFYA One-Press® is given by injection under your skin (subcutaneous injection).

You and your healthcare professional should decide if you should inject TREMFYA®/TREMFYA One-Press® yourself. It is important not to try to inject yourself until you have been trained by your healthcare professional. A caregiver may also give you your TREMFYA®/TREMFYA One-Press® injection after proper training.

Before use, remove TREMFYA®/TREMFYA One-Press® from the refrigerator. Keep TREMFYA®/TREMFYA One-Press® inside the carton and allow it to reach room temperature by waiting for 30 minutes before injection.

**Read the “Instructions for Use” document carefully before using TREMFYA®/TREMFYA One-Press®.**

#### **Usual dose:**

Your doctor will decide how much TREMFYA®/TREMFYA One-Press® you need and for how long.

#### **Plaque Psoriasis**

- The dose is 100 mg (the contents of 1 pre-filled syringe or the contents of 1 patient-controlled injector) by subcutaneous injection.
- The first dose may be given by your healthcare provider.
- After the first dose, you will have the next dose 4 weeks later, and then every 8 weeks.

## Psoriatic Arthritis

- The dose is 100 mg (the contents of 1 pre-filled syringe or the contents of 1 patient-controlled injector) by subcutaneous injection.
- The first dose may be given by your healthcare provider.
- After the first dose, you will have the next dose 4 weeks later, and then every 8 weeks

TREMFYA®/TREMFYA One-Press® is for long-term treatment. Your healthcare professional will regularly monitor your condition to check that the treatment is having the desired effect.

You should not stop using TREMFYA®/TREMFYA One-Press® unless you think it is causing a severe side effect. Speak to your doctor as soon as possible if this happens.

### Overdose:

If you accidentally inject more TREMFYA®/TREMFYA One-Press® than you should or the dose has been given sooner than prescribed, inform your healthcare professional.

If you think you have taken too much TREMFYA®/TREMFYA One-Press®, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

### Missed dose:

If you forget to take your TREMFYA®/TREMFYA One-Press® dose, inject a dose as soon as you remember. Then, take your next dose at your regular scheduled time. If you are not sure what to do, contact your healthcare professional.

### What are possible side effects from using TREMFYA®/TREMFYA One-Press®?

As with all medicines, this medicine can cause side effects, although not everybody gets them.

Most of the following side effects are mild to moderate. If any of these side effects becomes severe, tell your healthcare professional.

Some side effects are very common (may affect more than 1 in 10 people)

- Infections of the nose, sinuses, or throat (e.g. common cold) or chest infections (bronchitis)

Some side effects are common (may affect up to 1 in 10 people):

- Redness, pain, irritation, swelling, bruising and/or itching at the injection site
- diarrhea
- headache
- joint pain
- increased level of liver enzymes in the blood

Some side effects are uncommon (may affect up to 1 in 100 people):

- stomach flu (gastroenteritis)
- herpes simplex infections (e.g. cold sores, genital herpes)
- fungal infections of the skin (e.g. athlete's foot)
- migraine
- yeast infections
- allergic reactions
- skin rash
- decreased number of a type of white blood cell called neutrophils

These are not all the possible side effects you may feel when taking TREMFYA®/TREMFYA One-Press®. If you experience any side effects not listed here, contact your healthcare professional.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

### **Reporting Side Effects**

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

*NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.*

### **Storage:**

Store TREMFYA®/TREMFYA One-Press® in the refrigerator between 2°C to 8°C (36°F to 46°F).

Do not freeze. Do not use if TREMFYA®/TREMFYA One-Press® has been frozen.

Do not shake TREMFYA®/TREMFYA One-Press®.

Store in original packaging to protect from light until use.

Keep out of reach and sight of children.



**Do not use TREMFYA®/TREMFYA One-Press®:**

- if you notice that it is damaged or the seal is broken.
- if the liquid is discoloured, cloudy or you can see large particles floating in it.
- after the expiry date which is stated on the label and on the outer carton after “EXP.”

TREMFYA®/TREMFYA One-Press® is for single use only. Ask your healthcare professional how to throw away medicines no longer required.

**If you want more information about TREMFYA®/TREMFYA One-Press®:**

- Talk to your healthcare professional
- For questions or concerns, contact the manufacturer, Janssen Inc. ([www.janssen.com/canada](http://www.janssen.com/canada))
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>; the manufacturer’s website [www.janssen.com/canada](http://www.janssen.com/canada), or by contacting the manufacturer at: 1-800-567-3331 or 1-800-387-8781.

This leaflet was prepared by Janssen Inc., Toronto, Ontario, M3C 1L9.

Last Revised:

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## INSTRUCTIONS FOR USE (TREMFYA®)

PrTREMFYA®  
(guselkumab injection)

Pre-filled syringe



SINGLE-DOSE

### PLEASE READ THESE INSTRUCTIONS BEFORE USE

#### Important

TREMFYA® comes as a single-dose pre-filled syringe containing one 100 mg dose. Each pre-filled syringe can be used only one time. Throw the used pre-filled syringe away (see Step 3) after each dose, even if there is medicine left in it. Do not reuse your pre-filled syringe.

If your doctor decides that you or a caregiver may be able to give your injections of TREMFYA® at home, you should receive training on the right way to prepare and inject TREMFYA® using the pre-filled syringe before attempting to inject.

Read this Instructions for Use document before using the TREMFYA® pre-filled syringe and each time you get a refill. There may be new information. This instruction guide does not take the place of talking with your doctor about your medical condition or your treatment. Please also read the Package Insert carefully and discuss any questions you may have with your doctor or nurse.

The TREMFYA® pre-filled syringe is intended for injection under the skin, not into the muscle or vein. After injection, the needle will retract into the body of the device and lock into place.



#### Storage information

Store in refrigerator at 2° to 8°C. Do not freeze.

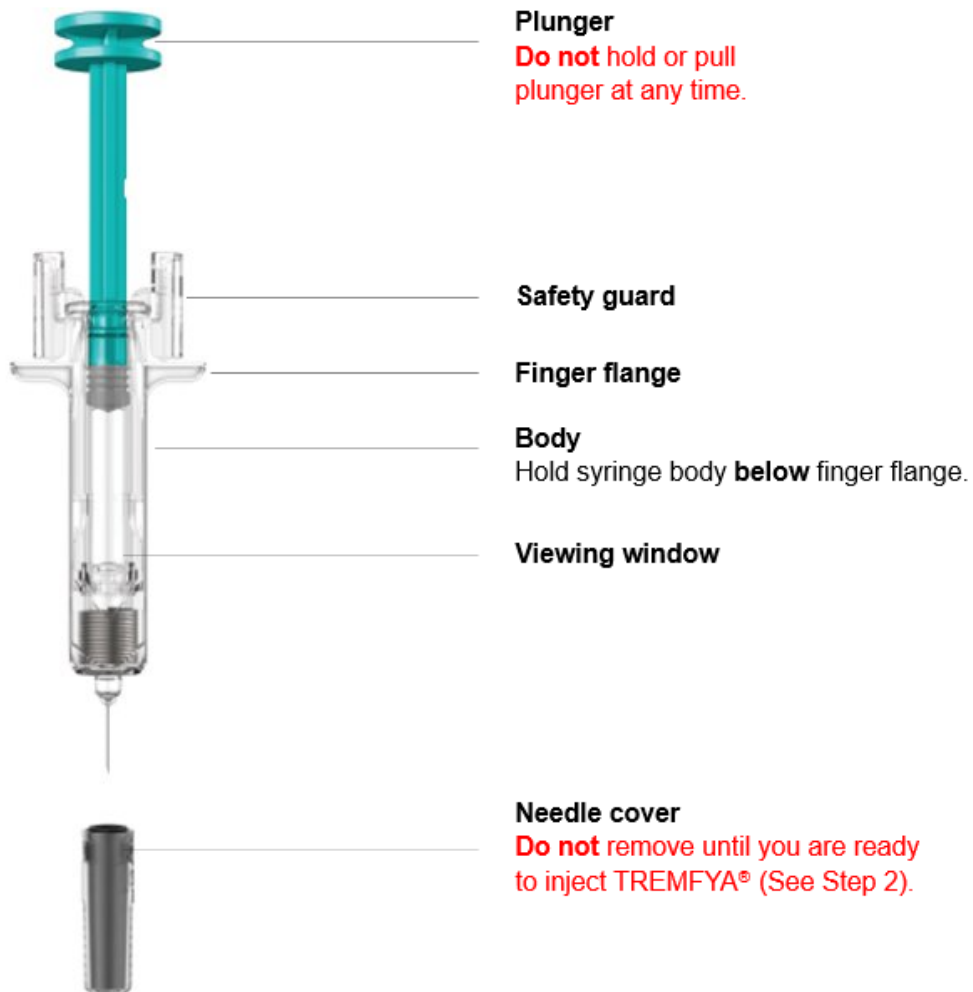
**Keep TREMFYA® and all medicines out of reach and sight of children.**

**Do not shake the pre-filled syringe.**

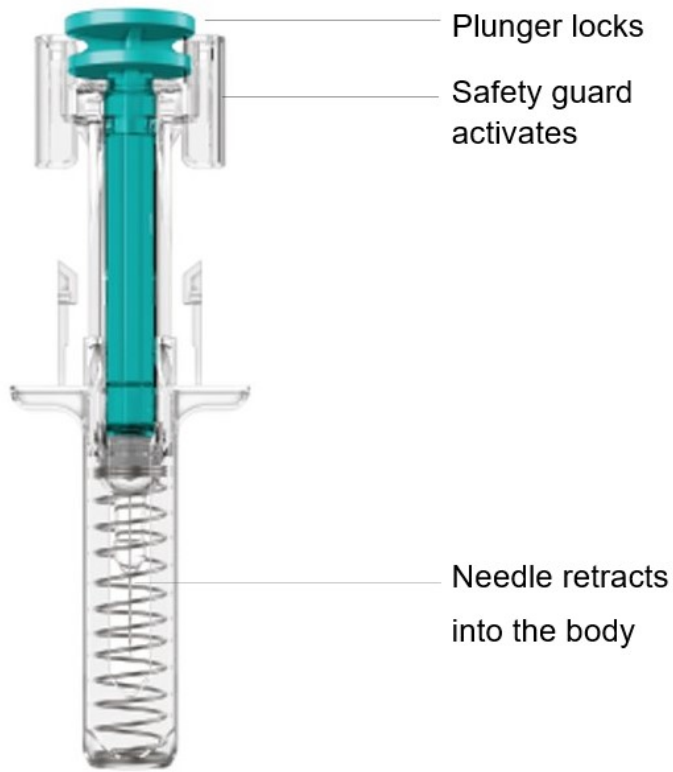
Keep TREMFYA® pre-filled syringe in the original carton to protect from light and physical damage.

### Pre-filled syringe parts

#### Before injection



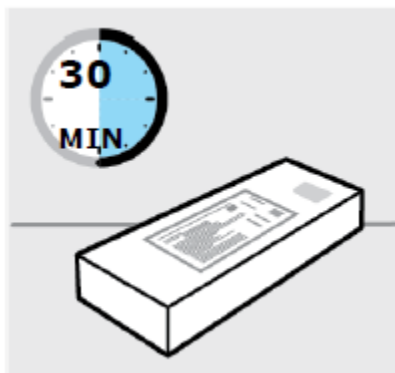
### After injection



### You will need these additional supplies:

- **1 Alcohol swab**
- **1 Cotton ball or gauze pad**
- **1 Adhesive bandage**
- **1 Sharps container (See Step 3)**

## 1. Prepare for your injection



### Inspect carton

Remove carton with the pre-filled syringe from the refrigerator.

Keep the pre-filled syringe in the carton and let it sit on a flat surface at room temperature for **at least 30 minutes** before use.

**Do not** warm any other way.

**Check the expiration date ('EXP')** on the back panel of the carton.

**DO NOT** use if the expiration date has passed.

**Do not** inject TREMFYA® if the perforations on the carton are broken.

Call your doctor or pharmacist for a refill.



### Choose injection site

Select from the following areas for your injection:

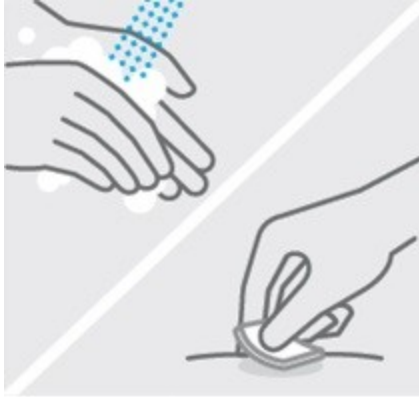
- **Front of thighs** (recommended)
- Lower abdomen

**Do not** use the 2-inch (5-centimetre) area around belly-button.

- Back of upper arms (if a caregiver is giving you the injection)

**DO NOT** inject into skin that is tender, bruised, red, scaly or hard.

**Do not** inject into areas with scars or stretch marks.

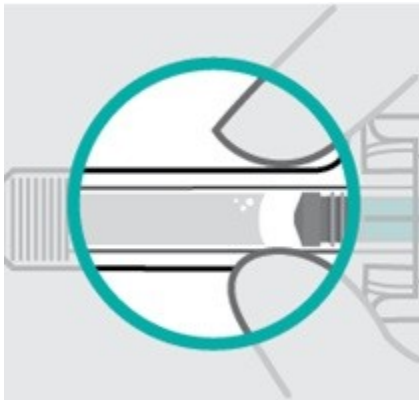


### **Clean injection site**

Wash your hands well with soap and warm water.

Wipe your chosen injection site with an alcohol swab and allow it to dry.

**Do not** touch, fan or blow on the injection site after you have cleaned it.



### **Inspect liquid**

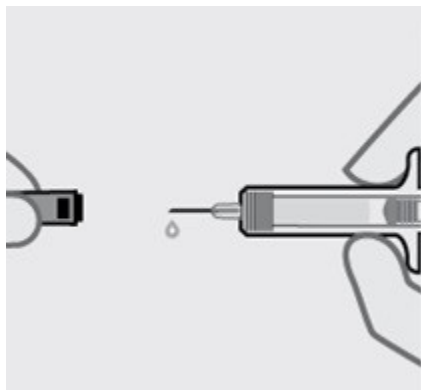
Take the pre-filled syringe out of the carton.

Check the liquid in the viewing window. It should be clear to slightly yellow and may contain tiny white or clear particles. You may also see one or more air bubbles.

This is normal.

**Do not** inject if the liquid is cloudy or discolored, or has large particles. Call your doctor or pharmacist for a refill.

## 2. Inject TREMFYA® using the pre-filled syringe



### Remove needle cover

Hold syringe by the body and pull needle cover straight off.

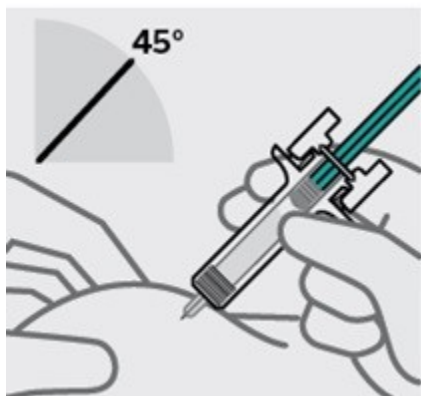
It is normal to see a drop of liquid.

**Inject within 5 minutes** of removing the needle cover.

**DO NOT** put needle cover back on, as this may damage the needle or cause a needle stick injury.

**DO NOT** touch needle or let it touch any surface.

**DO NOT** use the TREMFYA® pre-filled syringe if it is dropped. Call your doctor or pharmacist for a refill.



### Position fingers and insert needle

Place your thumb, index and middle fingers **directly under the finger flange**, as shown.

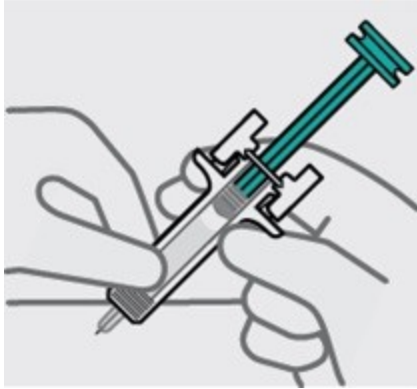
**Do not** touch plunger or area above finger flange as this may cause the needle safety device to activate.

Use your other hand to pinch skin at the injection site.

Position syringe at about a 45 degree angle to the skin.

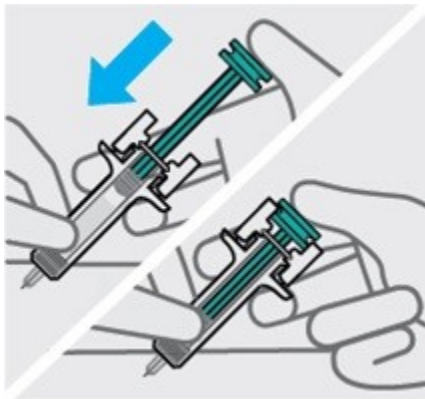
It is important to pinch enough skin to **inject under the skin** and not into the muscle.

Insert needle with a quick, dart-like motion.



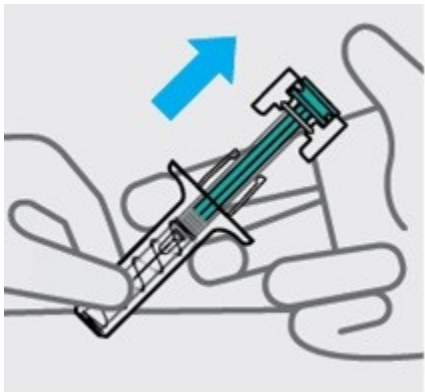
**Release pinch and reposition hand**

Use your free hand to grasp the body of the syringe.



**Press plunger**

Place thumb from the opposite hand on the plunger and press the plunger **all the way down until it stops**.



**Release pressure from plunger**

The safety guard will cover the needle and lock into place, removing the needle from your skin.



### 3. After your injection

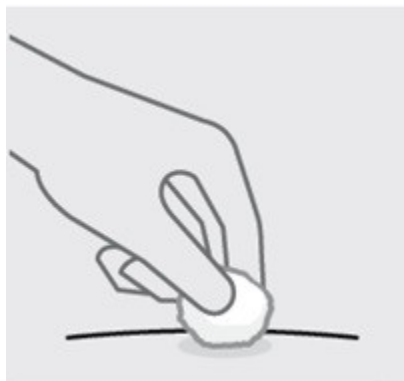


#### **Throw the used pre-filled syringe away**

Put your used syringe in a sharps disposal container right away after use.

**Do not** dispose in your household trash.

Make sure you dispose of the bin as instructed by your doctor or nurse when the container is full.



#### **Check injection site**

There may be a small amount of blood or liquid at the injection site. Hold pressure over your skin with a cotton ball or gauze pad until any bleeding stops.

**Do not** rub the injection site.

If needed, cover injection site with a bandage.



#### **Need Help?**

Call your doctor to talk about any questions you may have. For questions or concerns visit the manufacturer's website [www.janssen.com/canada](http://www.janssen.com/canada), or call 1-800-567-3331 or 1-800-387-8781.

This leaflet was prepared by Janssen Inc., Toronto, Ontario, M3C 1L9.

Last Revised

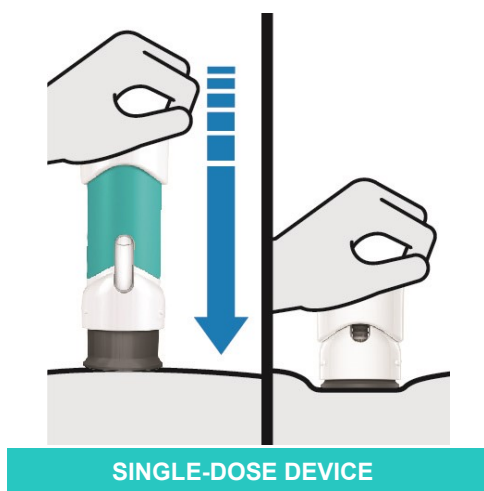
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## INSTRUCTIONS FOR USE (TREMFYA One-Press®)

P<sup>r</sup>TREMFYA One-Press®

(guselkumab injection)

100 mg patient-controlled injector



### Important

TREMFYA One-Press® comes as a single-dose patient-controlled injector containing one 100 mg dose. Each One-Press injector can only be used one time. Throw away (see Step 3) after each dose, even if there is medicine left in it. Do not reuse your One-Press injector.

If your doctor decides that you or a caregiver may be able to give your injections of TREMFYA One-Press® at home, you should receive training on the right way to prepare and inject TREMFYA One-Press®.

Please read these Instructions for use before using the TREMFYA One-Press® and each time you fill your prescription. There may be new information. This instruction guide does not take the place of talking with your doctor about your medical condition or your treatment.

Please also read the Package Insert carefully before starting your injection and discuss any questions you may have with your doctor or nurse.

**During injection, push handle all the way down until teal body is not visible to inject the full dose.**

**DO NOT LIFT THE ONE-PRESS INJECTOR during injection. If you do, the One-Press injector will lock and you will not get the full dose.**



### Storage information

Store in refrigerator at 2° to 8°C.

**Do not** freeze.

**Do not** shake at any time.

**Keep TREMFYA One-Press® and all medicines out of reach and sight of children.**

**Keep TREMFYA One-Press® in the original carton to protect from light and physical damage.**

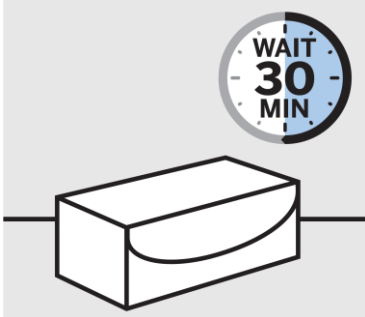
### TREMFYA One-Press® at-a-glance



#### You will need these supplies:

- 1 Alcohol swab
- 1 Cotton ball or gauze pad
- 1 Adhesive bandage
- 1 Sharps container (See Step 3)

## 1. Prepare for your injection

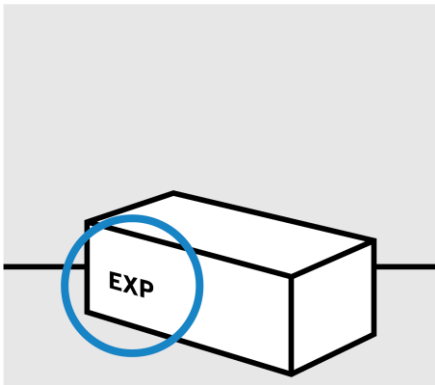


### **Inspect carton and allow TREMFYA One-Press® to come to room temperature**

Remove carton with TREMFYA One-Press® from the refrigerator.

Keep TREMFYA One-Press® in the carton and let it sit on a flat surface at room temperature for **approximately 30 minutes** before use.

**Do not** warm any other way.



### **Check the expiration date ('EXP') on the carton.**

**Do not** use if the expiration date has passed.

**Do not** inject if the seal on the carton is broken.

Call your doctor or pharmacist for a new TREMFYA One-Press®.



### Choose injection site

Select from the following areas for your injection:

- **Front of thighs** (recommended)
- Lower abdomen
  - **Do not** use the 2-inch (5-centimetre) area around your belly-button.
- Back of upper arms (if a caregiver is giving you the injection)

**Do not** inject into skin that is tender, bruised, red, scaly, hard or has scars or stretch marks.



### Wash hands

Wash your hands well with soap and warm water.

### Clean injection site

Wipe your chosen injection site with an alcohol swab and allow it to dry.

**Do not** touch, fan or blow on the injection site after you have cleaned it.



### Inspect liquid in window

Take **TREMFYA One-Press®** out of the carton.

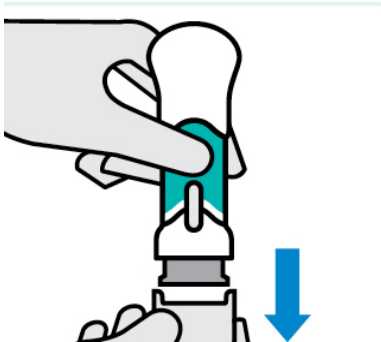
Check the liquid in the window. It should be clear to slightly yellow and may contain tiny white or clear particles. You may also see one or more air bubbles. This is normal.

**Do not** inject if the liquid is:

- cloudy, or
- discoloured, or
- has large particles.

If you are uncertain, call your doctor or pharmacist for a new **TREMFYA One-Press®**.

## 2. Inject TREMFYA One-Press® using the patient-controlled injector



### Pull off bottom cap when you are ready to inject

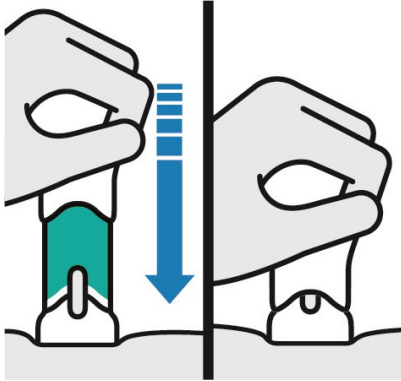
Keep hands away from the needle guard after the cap is removed. It is normal to see a few drops of liquid.

**Inject within 5 minutes of removing the cap.**

**Do not** put the cap back on. This could damage the needle.

**Do not** use the product if it is dropped after removing the cap.

Call your doctor or pharmacist for a new **TREMFYA One-Press®**.



**Place straight on skin**

**Push handle all the way down until teal body is not visible**

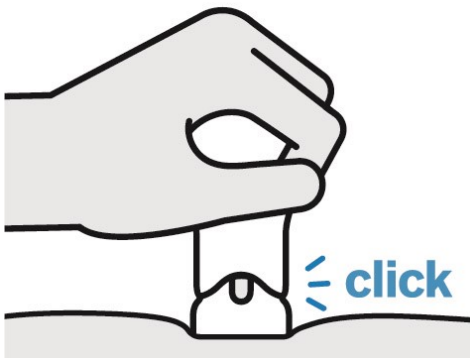
**DO NOT LIFT THE ONE-PRESS INJECTOR DURING THE INJECTION!**

If you do, the needle guard will lock, showing a yellow band, and you will not get the full dose.

You may hear a click when the injection begins. Keep pushing.

**If you feel resistance, keep pushing. This is normal.**

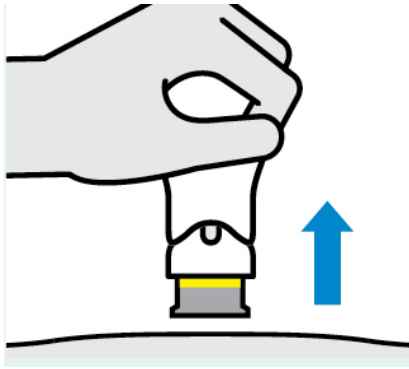
The medication injects as you push. Do this at a speed that is comfortable for you.



**Confirm injection is complete**

Injection is complete when:

- **The teal body is no longer visible**
- You cannot press the handle down anymore
- You may hear a click



### **Lift straight up**

The yellow band indicates that the needle guard is locked.

## **3. After your injection**



### **Throw the used product away**

Put your used product in a sharps disposal container right away after use.

Make sure you dispose of the bin as instructed by your doctor or nurse when the container is full.

**Do not** throw away (dispose of) your product in your household waste.

**Do not** recycle your used sharps disposal container.





### **Check injection site**

There may be a small amount of blood or liquid at the injection site. Hold pressure over your skin with a cotton ball or gauze pad until any bleeding stops. **Do not** rub the injection site. If needed, cover injection site with a bandage.



### **Need Help?**

Call your doctor to talk about any questions you may have. For questions or concerns visit the manufacturer's website [www.janssen.com/canada](http://www.janssen.com/canada), or call 1-800-567-3331 or 1-800-387-8781.

This leaflet was prepared by Janssen Inc., Toronto, Ontario, M3C 1L9.

Last Revised:

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