PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PrTREMFYA®

guselkumab injection
Solution for injection

PrTREMFYA®
100 mg/1 mL Pre-filled syringe
200 mg/2 mL Pre-filled syringe
200 mg/2 mL Pre-filled pen

PrTREMFYA One-Press®
100 mg/1 mL Patient-controlled injector

PrTREMFYA® I.V.

guselkumab for injection
Solution for intravenous infusion,
200 mg/20 mL vial

Interleukin-23 (IL-23) inhibitor

ATC L04AC16

TREMFYA®/TREMFYA® I.V. (guselkumab injection/guselkumab for injection) should be prescribed by physicians who have sufficient knowledge of plaque psoriasis, psoriatic arthritis, ulcerative colitis or Crohn's disease and who have fully familiarized themselves with the efficacy/safety profile of the drug.

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RECENT MAJOR LABEL CHANGES

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PART I: HEALTH PROFESSIONAL INFORMATION

Guselkumab administered subcutaneously will be referred to throughout the Product Monograph as TREMFYA®. Guselkumab administered through intravenous infusion will be referred to throughout the Product Monograph as TREMFYA® I.V.

1 INDICATIONS

Plaque Psoriasis

TREMFYA® (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® (guselkumab injection) is indicated for:

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

Crohn's disease

TREMFYA®/TREMFYA® I.V. (guselkumab injection/guselkumab for injection) is indicated for:

- the treatment of adult patients with moderately to severely active Crohn's disease.

Ulcerative Colitis

TREMFYA®/TREMFYA® I.V. (guselkumab injection/guselkumab for injection) is indicated for:

- the treatment of adult patients with moderately to severely active ulcerative colitis.

1.1 Pediatrics

The safety and efficacy of TREMFYA®/TREMFYA® I.V. in pediatric patients have not been evaluated.

1.2 Geriatrics

Of the 3406 plaque psoriasis and psoriatic arthritis patients exposed to TREMFYA® 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%). Of the 1089 Crohn's disease patients exposed to TREMFYA®/TREMFYA® I.V. in clinical trials, 40 were 65 years or older, and 5 were 75 years or older. Of the 897 ulcerative colitis patients exposed to TREMFYA®/TREMFYA® I.V. in clinical trials, 55 were 65 years or older, and 10 were 75 years or older. Thus, data in these age groups are limited (see 10 CLINICAL PHARMACOLOGY).

2 CONTRAINDICATIONS

TREMFYA®/TREMFYA® I.V. 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® is administered by subcutaneous injection. TREMFYA® I.V. is administered by intravenous infusion.

4.1 Dosing Considerations

TREMFYA®/TREMFYA® I.V. is intended for use under the guidance and supervision of a physician.

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

The BioAdvance® Network has been established to facilitate the administration of TREMFYA®/TREMFYA® I.V. BioAdvance® clinics are staffed by qualified healthcare professionals specially trained in the administration of TREMFYA®/TREMFYA® I.V. and care of patients with Crohn's disease or ulcerative colitis. BioAdvance® clinics are available across Canada. Information about the BioAdvance® Network and location of the nearest BioAdvance® Network clinic can be obtained by calling Janssen Inc. Medical Information at: 1-800-567-3331.

4.2 Recommended Dose and Dosage Adjustment

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

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

Crohn's disease
Induction:
The recommended induction dosage is:

- 200 mg of TREMFYA® I.V. administered by intravenous infusion over a period of at least one hour at Week 0, Week 4 and Week 8.

or

- 400 mg of TREMFYA® administered by subcutaneous injection at Week 0, Week 4 and Week 8. Each 400 mg dose is given as two injections of 200 mg

Maintenance:
The recommended maintenance dosage is 100 mg of TREMFYA® administered by subcutaneous injection at Week 16 and every 8 weeks thereafter.

A dose of 200 mg administered by subcutaneous injection at Week 12 and every 4 weeks thereafter may be considered for patients who do not show adequate therapeutic benefit to guselkumab, or according to clinical judgement (see 14 CLINICAL TRIALS).

Immunomodulators and/or corticosteroids may be continued during treatment with TREMFYA®. In patients who have responded to treatment with TREMFYA®, corticosteroids may be reduced or discontinued in accordance with standard of care.

Ulcerative colitis
Induction:
The recommended induction dosage is 200 mg of TREMFYA® I.V. administered by intravenous infusion over a period of at least one hour at Week 0, Week 4 and Week 8.

Maintenance:
The recommended maintenance dosage is 100 mg of TREMFYA® administered by subcutaneous injection at Week 16 and every 8 weeks thereafter after completion of induction dosing.

A dose of 200 mg administered by subcutaneous injection at Week 12 and every 4 weeks thereafter may be considered for patients who do not show adequate therapeutic benefit to guselkumab, or according to clinical judgement (see 14 CLINICAL TRIALS).

Immunomodulators and/or corticosteroids may be continued during treatment with TREMFYA®. In patients who have responded to treatment with TREMFYA®, corticosteroids may be reduced or discontinued in accordance with standard of care.

Special populations
Pediatrics (< 18 years of age)
The safety and efficacy of TREMFYA®/TREMFYA® I.V. 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® 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%). Of 1089 Crohn's disease patients exposed to TREMFYA®/TREMFYA® I.V. in clinical trials, 40 were 65 years or older, and 5 were 75 years or older. Of 897 ulcerative colitis patients exposed to TREMFYA®/TREMFYA® I.V. in clinical trials, 55 were 65 years or older, and 10 were 75 years or older. Thus, data in these age groups are limited (see 10 CLINICAL PHARMACOLOGY).

Renal impairment
Specific studies of TREMFYA®/TREMFYA® I.V. have not been conducted in patients with renal

insufficiency.

Hepatic impairment
Specific studies of TREMFYA®/TREMFYA® I.V. have not been conducted in patients with hepatic insufficiency.

4.4 Administration

Subcutaneous Administration (TREMFYA®)
TREMFYA® is administered by subcutaneous injection. TREMFYA® is intended for use under the guidance and supervision of a physician. TREMFYA® 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® should be injected according to the directions provided in the "Instructions for Use" document.

Before injection, remove TREMFYA® from the refrigerator and allow TREMFYA® to reach room temperature (30 minutes) without removing from the carton.

Inspect TREMFYA® visually for particulate matter and discoloration prior to administration. TREMFYA® 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.

Intravenous Infusion (TREMFYA® I.V.)
TREMFYA® I.V. is for IV infusion only. Intravenous infusion of TREMFYA® I.V. should be administered by qualified healthcare professionals.

TREMFYA® I.V. solution for intravenous infusion must be diluted, prepared and infused by a healthcare professional using aseptic technique. TREMFYA® I.V. does not contain preservatives. Each vial is for single use only.

Inspect TREMFYA® I.V. visually for particulate matter and discoloration prior to administration. TREMFYA® I.V. is a clear and colorless to light yellow solution that may contain small translucent particles. Do not use if the liquid contains large particles, is discolored or cloudy. Add TREMFYA® I.V. to a 250 mL intravenous infusion bag of 0.9% Sodium Chloride Injection as follows:

1. Withdraw and then discard 20 mL of the 0.9% Sodium Chloride Injection from the 250 mL infusion bag which is equal to the volume of TREMFYA® I.V. to be added.
2. Withdraw 20 mL of TREMFYA® I.V. from the vial and add it to the 250 mL intravenous infusion bag of 0.9% Sodium Chloride Injection for a final concentration of 0.8 mg/mL. Gently mix the diluted solution. Discard the vial with any remaining solution.
3. Visually inspect the diluted solution for particulate matter and discoloration before infusion. Infuse the diluted solution over a period of at least one hour.
4. Use only an infusion set with an in-line, sterile, non-pyrogenic, low protein binding filter (pore size 0.2 micrometer).
5. Do not infuse TREMFYA® I.V. concomitantly in the same intravenous line with other medicinal products.

6. Dispose any unused medicinal product in accordance with local requirements.

4.5 Missed Dose

Patients who miss a dose of TREMFYA® 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

Intravenous doses up to 1200 mg as well as subcutaneous doses up to 400 mg at a single dosing visit have been administered in clinical studies 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 the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

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: 200 mg / 2mL (100 mg / mL), 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
Subcutaneous Injection (SC)	Sterile solution for injection in a single-dose pen: 200 mg / 2mL (100 mg / mL)	L-histidine, L-histidine monohydrochloride monohydrate, polysorbate 80, sucrose and water for injection
Intravenous Infusion (IV)	Sterile solution in single-use vial: 200 mg / 20 mL (10 mg / mL)	EDTA disodium dihydrate, L-histidine, L-histidine monohydrochloride monohydrate, L-methionine, polysorbate 80, sucrose and water for injection

TREMFYA®/TREMFYA® I.V. (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®

TREMFYA® is supplied as:

- Pre-filled syringe: A sterile solution in a single-dose glass syringe with a 27G, half inch fixed needle assembled in a passive needle guard delivery system packaged in a carton, containing:
  - 100 mg guselkumab (100 mg/mL in a 1 mL syringe volume)
  - 200 mg guselkumab (100 mg/mL in a 2 mL syringe volume)
- Pen: A sterile solution in a single-dose glass syringe with a 27G, half-inch fixed needle assembled in a pre-filled pen packaged in a carton, containing:
  - 200 mg guselkumab (100 mg/mL in a 2 mL syringe volume)
- TREMFYA One-Press®: A sterile solution in a single-dose glass syringe with a 27G, half inch fixed needle assembled in a patient-controlled injector packaged in a carton, containing:
  - 100 mg guselkumab (100 mg/mL in a 1 mL volume)

TREMFYA® does not contain preservatives.

The TREMFYA® pre-filled syringe, pen, and TREMFYA One-Press® needle guard and plunger stopper are not made with natural rubber latex.

TREMFYA® I.V.

TREMFYA® I.V. is supplied as a sterile solution for intravenous infusion in a single-use type 1 glass vial containing 200 mg guselkumab (10 mg/mL in a 20 mL volume) packaged in a carton.

TREMFYA® I.V. does not contain preservatives.

7 WARNINGS AND PRECAUTIONS

General

Infections

TREMFYA®/TREMFYA® I.V. 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). A similar risk of infection was seen in the placebo-controlled trials in patients with Crohn's disease and in patients with ulcerative colitis. The most common type of infection reported was respiratory tract infection (See 8 ADVERSE REACTIONS, Infections).

Treatment with TREMFYA®/TREMFYA® I.V. 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® I.V. 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® I.V. until the infection resolves.

Tuberculosis

Evaluate patients for TB infection prior to initiating treatment with TREMFYA®/TREMFYA® I.V. Initiate treatment of latent TB prior to administering TREMFYA®/TREMFYA® I.V. Patients receiving TREMFYA®/TREMFYA® I.V. should be monitored for signs and symptoms of active TB during and after treatment. Do not administer TREMFYA®/TREMFYA® I.V. to patients with active TB infection. Consider anti-TB therapy prior to initiating TREMFYA®/TREMFYA® I.V. 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® I.V., consider completion of all age appropriate immunizations according to current immunization guidelines. Avoid use of live vaccines in patients treated with TREMFYA®/TREMFYA® I.V. (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® I.V. 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 (AUC_{last} was 43-fold greater than the human exposure following a dose of 200 mg given subcutaneously). This observation was not repeated in a second male fertility study. No effects were observed at 25 mg/kg (AUC_{last} was 10-fold greater 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® I.V. should be discontinued.

7.1 Special Populations

7.1.1 Pregnant Women

The use of TREMFYA®/TREMFYA® I.V. in pregnant women has not been studied. The effect of TREMFYA®/TREMFYA® I.V. 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 (AUC_{last} was 7-fold greater than human levels following a dose of 200 mg given subcutaneously). 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® I.V. and for at least 12 weeks after the last TREMFYA®/TREMFYA® I.V. dose. TREMFYA®/TREMFYA® I.V. 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®/TREMFYA® I.V. 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® I.V. in pediatric patients have not been evaluated.

7.1.4 Geriatrics

Of the 3406 plaque psoriasis and psoriatic arthritis patients exposed to TREMFYA® 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%). Of 1089 Crohn's disease patients exposed to TREMFYA®/TREMFYA® I.V. in clinical trials, 40 were 65 years or older, and 5 were 75 years or older. Of 897 ulcerative colitis patients exposed to TREMFYA®/TREMFYA® I.V. in clinical trials, 55 were 65 years or older, and 10 were 75 years or older. 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.

In the pooled Phase 2/3 GALAXI studies in Crohn's disease, the proportion of TREMFYA® I.V.-treated patients who discontinued treatment due to adverse events was 1.7% (11/649) compared to 4.3% (9/211) in placebo-treated patients through 12 weeks. Serious adverse events were reported in 2.9% (19/649) of TREMFYA® I.V.-treated patients and 6.2% (13/211) of placebo-treated patients through 12 weeks.

In the 12-week phase 3 induction study in ulcerative colitis, the proportion of TREMFYA® I.V.-treated patients who discontinued treatment due to adverse events was 1.7% (7/421) compared to 3.9% (11/280) in placebo-treated patients. Serious adverse events were reported in 2.9% (12/421) of TREMFYA® I.V.-treated patients and 7.1% (20/280) of placebo-treated patients through 12 weeks.

Overall, the safety profile of TREMFYA®/TREMFYA® I.V. 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® in plaque psoriasis and psoriatic arthritis 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®-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® 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.

The safety profile of TREMFYA®/TREMFYA® I.V. in Crohn's disease is based on data from the Phase 2 (GALAXI 1) and Phase 3 (GALAXI 2, GALAXI 3, GRAVITI) studies in 1089 patients with Crohn's disease.

The safety profile of TREMFYA®/TREMFYA® I.V. in ulcerative colitis is based on data from Phase 2 (QUASAR induction dose-ranging study) and Phase 3 (Quasar induction study [IS] and QUASAR maintenance study [MS]) studies in 897 patients with ulcerative colitis.

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

[a] Subjects received 100 mg of TREMFYA® at Week 0, Week 4, and every 8 weeks thereafter;
[b] Subjects received adalimumab at 80 mg Week 0, 40 mg week 1 then 40 mg q2w thereafter
[c] Injection site reactions include injection site erythema, bruising, hematoma, hemorrhage, swelling, edema, pruritus, pain,discoloration, induration, inflammation, and urticaria.
[d] Upper respiratory infections include nasopharyngitis, upper respiratory tract infection (URTI), pharyngitis, and viral URTI.
[e] Gastroenteritis includes gastroenteritis and viral gastroenteritis
[f] Herpes simplex infections include oral herpes, herpes simplex, genital herpes, genital herpes simplex, and nasal herpes simplex.
[g] Tinea infections include tinea pedis, tinea cruris, tinea infection, and tinea manuum infections.
[h] 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[a] N = 375 n (%)	TREMFYA® q4w[b] N = 373 n (%)
Gastrointestinal disorders			
Diarrhea	3 (0.8%)	6 (1.6%)	4 (1.1%)
General disorders and administration site conditions			
Injection site reactions[c]	1 (0.3%)	5 (1.3%)	3 (0.8%)
Infections and Infestations			
Respiratory tract infections[d]	45 (12.1%)	46 (12.3%)	52 (13.9%)
Investigations			
Transaminases increased[e]	17 (4.6%)	31 (8.3%)	32 (8.6%)
Neutrophil count decreased [f]	3 (0.8%)	7 (1.9%)	7 (1.9%)
Nervous system disorders			
Headache[g]	3 (0.8%)	8 (2.1%)	7 (1.9%)

[a] Patients received 100 mg of TREMFYA® at Week 0, Week 4, and every 8 weeks thereafter
[b] Patients received 100 mg of TREMFYA® at Week 0, Week 4, and every 4 weeks thereafter
[c] Injection site reactions include injection site erythema, bruising, hematoma, hemorrhage, swelling, edema, pruritus, pain, discoloration, induration, inflammation, and urticaria.
[d] Respiratory tract infections include nasopharyngitis, upper respiratory tract infection (URTI), bronchitis, pharyngitis, and viral URTI.
[e]Transaminases increased includes alanine aminotransferase increased, aspartate aminotransferase increased, hepatic enzyme increased, transaminases increased, liver function test abnormal, hypertransaminasaemia
[f] Neutrophil count decreased includes neutrophil count decreased and neutropenia
[g] 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.

Adverse Drug Reactions in Crohn's Disease Trials

GALAXI

The clinical trials GALAXI 1, GALAXI 2, and GALAXI 3 enrolled 1349 patients, of whom 649 patients were randomized to receive TREMFYA® I.V. 200 mg by IV infusion at Week 0, 4 and 8 followed by a maintenance dose of either TREMFYA® 200 mg SC at Week 12 and every 4 weeks thereafter or TREMFYA® 100 mg SC at Week 16 and every 8 weeks thereafter.

Table 3 provides a summary of adverse reactions that occurred at a rate of at least 3% and at a higher rate in the TREMFYA®/TREMFYA® I.V. group than in the placebo group through Week 48 in the pooled analysis.

Table 3: Adverse Reactions Occurring in ≥3% of Patients through Week 48 in GALAXI 1, GALAXI 2, and GALAXI 3

	Placebo N=211 n (%)	**TREMFYA® I.V. 200 mg → 100 mg q8w SC N=353 n (%)**	**TREMFYA® I.V. 200 mg → 200 mg q4w SC N=296 n (%)**
Gastrointestinal disorders			
Diarrhea	3 (1.4%)	12 (3.4%)	8 (2.7%)
General disorders and administration site conditions			
Injection site reactions[a]	0	11 (3.1%)	10 (3.4%)
Infections and Infestations			
Respiratory tract infections[b]	30 (14.2%)	97 (27.5%)	100 (33.8%)
Gastroenteritis[c]	2 (0.9%)	10 (2.8%)	9 (3.0%)
Investigations			
Transaminases increased[d]	3 (1.4%)	11 (3.1%)	11 (3.7%)
Musculoskeletal and connective tissue disorders			
Arthralgia	8 (3.8%)	29 (8.2%)	25 (8.4%)
Nervous system disorders			
Headache[e]	6 (2.8%)	17 (4.8%)	24 (8.1%)
Skin and subcutaneous tissue disorders			
Rash[f]	4 (1.9%)	8 (2.3%)	10 (3.4%)

[a] Injection site reactions includes injection site erythema, injection site bruising, injection site haematoma, injection site haemorrhage, injection site swelling, injection site oedema, injection site pruritus, injection site pain, injection site discolouration, injection site induration, injection site inflammation, injection site urticaria.

[b] Respiratory tract infections includes nasopharyngitis, upper respiratory tract infection (URTI), bronchitis, pharyngitis, viral URTI, COVID-19, influenza.
[c] Gastroenteritis includes gastroenteritis, gastroenteritis viral
[d] Transaminases increased includes alanine aminotransferase increased, aspartate aminotransferase increased, hepatic enzyme increased, transaminases increased, liver function test abnormal, hypertransaminasaemia.
[e] Headache includes headache, tension headache.
[f] Rash includes rash, rash erythematous, rash papular, rash pruritic.

GRAVITI

The clinical trial GRAVITI evaluated 347 patients, of whom 230 patients were randomized to receive TREMFYA® 400 mg SC at Week 0, 4 and 8 followed by a maintenance dose of either TREMFYA 200 mg SC at Week 12 and every 4 weeks thereafter or TREMFYA 100 mg SC at Week 16 and every 8 weeks thereafter.

Table 4 provides a summary of adverse reactions that occurred at a rate of at least 3% and at a higher rate in the TREMFYA®/TREMFYA® I.V. group than in the placebo group through Week 48.

Table 4: Adverse Reactions Occurring in ≥3% of Patients through Week 48 in GRAVITI

	Placebo N=117 n (%)	TREMFYA 400 mg SC Induction→ 100 mg q8w SC N=115 n (%)	TREMFYA 400 mg SC Induction→ 200 mg q4w SC N=115 n (%)
Gastrointestinal disorders			
Diarrhea	3 (2.6%)	6 (5.2%)	4 (3.5%)
Infections and Infestations			
Respiratory tract infections[a]	29 (24.8%)	38 (33.0%)	35 (30.4%)
Gastroenteritis[b]	1 (0.9%)	5 (4.3%)	3 (2.6%)
Musculoskeletal and connective tissue disorders			
Arthralgia	4 (3.4%)	6 (5.2%)	5 (4.3%)
Nervous system disorders			
Headache[c]	5 (4.3%)	7 (6.1%)	9 (7.8%)

[a] Respiratory tract infections includes nasopharyngitis, upper respiratory tract infection (URTI), bronchitis, pharyngitis, viral URTI, COVID-19, influenza.
[b] Gastroenteritis includes gastroenteritis, gastroenteritis viral
[c] Headache includes headache, tension headache.

Adverse Drug Reactions in Ulcerative Colitis Trials

Adverse reactions that occurred at a rate of at least 2% and at a higher rate in the TREMFYA® I.V. group than in the placebo group during the 12-week induction studies QUASAR induction dose-ranging study and QUASAR IS were rash (includes rash erythematous, rash papular, and rash pruritic).

Table 5 provides a summary of adverse reactions that occurred at a rate of at least 3% and at a higher rate in the TREMFYA® group than in the placebo group during the 44-week maintenance study QUASAR-MS.

Table 5 Adverse reactions reported by ≥3% of patients through Week 44 in QUASAR-MS

	Placebo N = 192 n (%)	TREMFYA® 100 mg Q8w[a] N = 186 n (%)	TREMFYA®. 200 mg Q4w[b] N = 190 n (%)
General disorders and administration site conditions			
Injection site reactions[c]	2 (1.0%)	2 (1.1%)	9 (4.7%)
Infections and Infestations			
Respiratory tract infections[d]	18 (9.4%)	15 (8.1%)	26 (13.7%)
Gastroenteritis[e]	3 (1.6%)	2 (1.1%)	6 (3.2%)
Musculoskeletal and connective tissue disorders			
Arthralgia	13 (6.8%)	8 (4.3%)	15 (7.9%)

[a] TREMFYA® 100 mg as a subcutaneous injection every 4 weeks after the induction regimen
[b] TREMFYA® 200 mg as a subcutaneous injection every 4 weeks after the induction regimen.
[c] Injection site reactions includes: Injection site erythema, injection site bruising, injection site hematoma, injection site hemorrhage, injection site swelling, injection site edema, injection site pruritus, injection site pain, injection site discolouration, injection site induration, injection site inflammation, injection site urticaria.
[d] Respiratory tract infections includes: nasopharyngitis, upper respiratory tract infection, bronchitis, pharyngitis, viral upper respiratory tract infection.
[e] Gastroenteritis includes: Gastroenteritis, Gastroenteritis viral.

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). A similar risk of infection was seen in the placebo-controlled trials in patients with Crohn's disease and in patients with ulcerative colitis.

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.

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 6). 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 6: Frequency of patients with transaminase increases post-baseline in two Phase III psoriatic arthritis clinical studies

	Through Week 24[a]			**Through 1 Year[b]**	
	Placebo N=370[d]	TREMFYA® 100 mg q8w N=373[d]	TREMFYA® 100 mg q4w[c] N=371[d]	TREMFYA® 100 mg q8w N=373[d]	TREMFYA® 100 mg q4w[c] N=371[d]
ALT					
>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%
AST					
>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%

[a] placebo-controlled period
[b] patients randomized to placebo at baseline and crossed over to TREMFYA® are not included
[c] q4w dosing is not recommended in psoriatic arthritis patients
[d] number of patients with at least one post-baseline assessment for the specific laboratory test within the time period

In pooled Phase 2/3 Crohn's disease clinical studies, through the reporting period of approximately one-year, adverse events of increased transaminases (includes ALT increased, AST increased, hepatic enzyme increased, transaminases increased, hepatic function abnormal, and liver function test increased) were reported in 3.4% of patients in the TREMFYA® 200 mg SC q4w treatment group and 4.1% of patients in the TREMFYA® 100 mg SC q8w treatment group compared to 2.4% in the placebo group. Based on laboratory assessments in pooled Phase 2/3 Crohn's disease clinical studies, the frequency of ALT or AST elevations were lower than those observed in psoriatic arthritis Phase 3 clinical studies. Through the reporting period of approximately one-year, ALT or AST elevations ≥ 3x ULN were reported in 2.7% of patients in the TREMFYA® 200 mg SC q4w treatment group and 2.6% of patients in the TREMFYA® 100 mg SC q8w treatment group compared to 1.9% in the placebo group. In most cases, the increase in transaminases was transient and did not lead to discontinuation of treatment.

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 phase 3 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® I.V. (see 7 WARNINGS AND PRECAUTIONS, Immune)**.**

Immunosuppression Therapy

The safety and efficacy of TREMFYA®/TREMFYA® I.V. 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]-1β, 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®/TREMFYA® I.V. 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 IgG1λ monoclonal antibody (mAb) that binds selectively to the p19 subunit of interleukin 23 (IL-23) through the antigen binding site 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. In patients with Crohn's disease or ulcerative colitis, levels of IL-23 are elevated in the colon tissue.

Guselkumab binds Fc-gamma receptor 1 (CD64) through its Fc region and has demonstrated dual-binding to IL-23 and CD64 *in vitro*. Myeloid cells expressing CD64 have been shown to be a predominant source of IL-23 in inflamed tissue in psoriasis, Crohn's disease, and ulcerative colitis.

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.

In patients with Crohn's disease and ulcerative colitis, guselkumab treatment led to a decrease in inflammatory markers including CRP and fecal calprotectin through induction Week 12, which were sustained through one year of maintenance treatment. Serum protein levels of IL-17A, IL-22 and IFNγ were reduced as early as Week 4, and continued to decrease through induction Week 12. Guselkumab also reduced colon mucosal biopsy RNA levels of IL-17A, IL-22 and IFNγ at Week 12.

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.

Table 7: Summary of guselkumab pharmacokinetic parameters following a single-dose IV or SC administration in healthy participants

Dose	Mean Cmax (mcg/mL)	Median Tmax (days)	Mean $t_{1/2}$ (days)	Mean $AUC_{0-\infty}$ (mcg*day/mL)	Mean CL/F (for SC) or CL (for IV) (L/day)	Mean Vd/F (for SC) or Vd (for IV) (L)
100 mg SC	8.09	5.5	17	188	0.681	16.6
200 mg SC	15.9	5.0	19	491	0.455	12.1
200 mg IV	58.8	Not Applicable	24	855	0.249	8.26

Abbreviations: Cmax = Maximum observed serum concentration. Tmax = Time to reach maximum observed serum concentration. t1/2 terminal half-life. $AUC_{0-\infty}$ = Area under the serum concentration versus time curve from time zero to infinity. CL = clearance. CL/F apparent total systemic clearance after extravascular administration. Vd = Volume of distribution. Vd/F = apparent volume of distribution after extravascular administration.

Absorption:

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

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

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 (± SD) steady-state trough serum guselkumab concentrations in two Phase 3 studies were 1.15 ± 0.73 mcg/mL and 1.23 ± 0.84 mcg/mL.

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

In subjects with Crohn's disease, mean peak serum guselkumab concentration at Week 8 was 70.5 mcg/mL following the recommended intravenous induction dose regimen of TREMFYA® I.V. 200 mg at Weeks 0, 4, and 8. Following the recommended subcutaneous induction dose regimen of TREMFYA® 400 mg at Weeks 0, 4, and 8, mean peak serum concentration was estimated to be 27.7 mcg/mL in subjects with Crohn's disease. The total systemic exposure (AUC) after the recommended induction dose regimens was similar following subcutaneous and intravenous induction. Following subcutaneous maintenance dosing of 100 mg TREMFYA® every 8 weeks or 200 mg TREMFYA® every 4 weeks in subjects with Crohn's disease, mean steady-state trough serum guselkumab concentrations were approximately 1.2 mcg/mL and 10.1 mcg/mL, respectively.

In subjects with ulcerative colitis, mean peak serum guselkumab concentration at Week 8 was 68.3 mcg/mL following the recommended intravenous induction dose regimen of TREMFYA® I.V. 200 mg at Weeks 0, 4, and 8. Following subcutaneous maintenance dosing of 100 mg TREMFYA® every 8 weeks or 200 mg TREMFYA® every 4 weeks, mean steady-state

trough serum guselkumab concentrations at Week 44 were approximately 1.4 mcg/mL and 10.7 mcg/mL, respectively.

Distribution:

Based on population pharmacokinetic analyses, the apparent volume of distribution of guselkumab following subcutaneous administration was 13.5 L in subjects with plaque psoriasis,11.4 L in subjects with Crohn's disease, and 10.1 L in subjects with ulcerative colitis.

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:

Based on population pharmacokinetic analyses, the apparent clearance of guselkumab following subcutaneous administration was 0.516 L/day in subjects with plaque psoriasis, 0.568 L/day in subjects with Crohn's disease and 0.531 L/day in subjects with ulcerative colitis. Mean half-life ($T_{1/2}$) of guselkumab was approximately 17 days in healthy subjects, approximately 15 to 18 days in subjects with plaque psoriasis across studies, and approximately 17 days in patients with Crohn's disease and in patients with ulcerative colitis.

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, azathioprine, and 6-mercaptopurine 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:** Population pharmacokinetic analyses indicated there were no apparent changes in clearance estimate in subjects ≥ 65 years of age compared to subjects < 65 years of age, suggesting no dose adjustment is needed for elderly patients. 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. 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. Of the 1009 Crohn's disease patients exposed to TREMFYA®/TREMFYA® I.V. in clinical studies and included in the pop PK analysis, a total of 39 patients were 65 years of age or older, including 5 patients were 75 years of age or older. Of the 859 ulcerative colitis patients exposed to TREMFYA®/TREMFYA® I.V. in clinical studies and included in the pop PK analysis, a total of 52 patients were 65 years of age or older, including 9 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.

10.4 Immunogenicity

As with all therapeutic proteins, there is the potential for immunogenicity with TREMFYA®/TREMFYA® I.V. The immunogenicity of TREMFYA®/TREMFYA® I.V. 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.

In patients with Crohn's disease in pooled Phase 2/3 (GALAXI) analyses up to Week 48, 5% (30/634) of subjects treated with guselkumab developed antidrug antibodies. Of these subjects who developed antidrug antibodies, 7% (2/30) had antibodies that were classified as neutralizing antibodies, which equates to 0.3% (2/634) of guselkumab-treated subjects. In a Phase 3 (GRAVITI) analysis up to Week 48, 9% (24/273) of subjects treated with guselkumab developed antidrug antibodies. Of these subjects who developed antidrug antibodies, 13% (3/24) had antibodies that were classified as neutralizing antibodies, which equates to 1% (3/273) of guselkumab-treated subjects. Most of the patients who were positive for antibodies to guselkumab had low titers. There were no identified clinically meaningful effects of antidrug antibodies on pharmacokinetics or effectiveness of guselkumab over the treatment duration of 48 weeks. A definitive conclusion regarding the impact of antidrug antibodies on the development of injection site reactions is precluded by the small number of participants who had an injection site reaction.

In pooled analyses of patients with ulcerative colitis in Phase 2/3 studies (QUASAR) up to Week 56 (n=501), 12% (n=58) of subjects treated with guselkumab developed antidrug antibodies. Of these subjects who developed antidrug antibodies, 16% (n=9) had antibodies that were classified as neutralizing which equates to 2% of all subjects treated with guselkumab. Most of the patients who were positive for antibodies to guselkumab had low titers. Overall, the small number of ulcerative colitis 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®/TREMFYA® I.V. with the incidences of antibodies to other products may be misleading.

11 STORAGE, STABILITY AND DISPOSAL

TREMFYA®/TREMFYA® I.V. is sterile and preservative-free. Discard any unused portion. 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.

Storage of diluted TREMFYA® I.V. infusion solution:

- The diluted infusion solution may be kept at room temperature up to 25°C (77°F) for up to 10 hours. Storage time at room temperature begins once the diluted solution has been prepared. The infusion should be completed within 10 hours after the dilution in the infusion bag.
- Do not freeze.
- Discard any unused portion of the infusion solution.

12 SPECIAL HANDLING INSTRUCTIONS

Following administration of TREMFYA®/TREMFYA® I.V., 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 IgG1λ mAb with an average molecular weight of 146,613 Daltons

Physicochemical properties: TREMFYA®/TREMFYA® I.V. (guselkumab injection/guselkumab for 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®
TREMFYA® is supplied as:

- Pre-filled syringe: sterile solution in a single-dose glass syringe with a fixed 27G, half inch needle assembled in a passive needle guard delivery system containing:
  - 100 mg guselkumab (100 mg/mL in a 1 mL syringe volume)
  - 200 mg guselkumab (100 mg/mL in a 2 mL syringe volume)
- Pen: sterile solution in a single-dose glass syringe with a 27G, half inch fixed needle assembled in a pre-filled pen containing:
  - 200 mg guselkumab (100 mg/mL in a 2 mL syringe volume)
- TREMFYA One-Press®: sterile solution in a single-dose glass syringe with a fixed 27G, half inch needle assembled in a patient-controlled injector.
  - 100 mg guselkumab (100 mg/mL in a 1 mL syringe volume)

TREMFYA® does not contain preservatives.

TREMFYA® I.V.

TREMFYA® I.V. is supplied as a sterile solution for intravenous infusion in a single-use type 1 glass vial containing 200 mg guselkumab (10 mg/mL in a 20 mL volume).

TREMFYA® I.V. does not contain preservatives.

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

Plaque Psoriasis

Table 8: 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[a] Adalimumab (n=334) SC 80 mg Week 0, 40 mg week 1 then 40 mg q2w.[b]	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[c] Placebo (n=248) SC Weeks 0, 4, 12 → guselkumab 100 mg SC Week 16, 20[a] Adalimumab (n=248) 80 mg Week 0, 40 mg week 1 then 40 mg q2w.[d]	992	43.0 (18-74)	M=692 F=300

[a] The placebo group crossed over to receive guselkumab at Weeks 16 and 20 then q8w
[b] All subjects, including those randomized to adalimumab at Week 0, received TREMFYA® 100 mg at Week 52 and every 8 weeks thereafter.
[c] 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.
[d] 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) ≥ 3, a Body Surface Area (BSA) involvement ≥ 10%, and Psoriasis Area and Severity Index (PASI) score ≥ 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 (TNFα) 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 9 and Table 10 below.

Table 9: Summary of Clinical Responses at Week 16 (NRI[a]) in Psoriasis Studies (Co-Primary Endpoints)

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

[a] Non-responder imputation.
[b] Treatment difference versus placebo adjusted by investigator site with Mantel-Haenszel weights.
[c] p-value < 0.001; p-value is based on the Cochran-Mantel-Haenszel chi-square test stratified by investigator site.

Table 10: Summary of Clinical Responses (NRI[a]) in Psoriasis Studies (Secondary Endpoints)

	VOYAGE 1			VOYAGE 2		
	TREMFYA®	**Adalimumab**	**Treatment**	**TREMFYA®**	**Adalimumab**	**Treatment**

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

[a] Non-Responder Imputation.
[b] Treatment difference versus adalimumab adjusted by investigator site with Mantel-Haenszel weights.
[c] 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® demonstrated superiority to placebo for the co-primary endpoints of IGA cleared (0) or minimal (1), and PASI 90 at week 16 (Table 9).

In addition, TREMFYA® 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 10). 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® 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® 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® or who crossed over from placebo, 460 patients received open-label TREMFYA® in the uncontrolled extension period after week 48. At week 252, 76.9% (380/494) of patients remained on TREMFYA® and 66.6% (329/494) achieved PASI 90.

In TREMFYA® 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 ≥ 2, 83.4% and 80.6% in the TREMFYA® 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® and who were PASI 90 responders at Week 28 in the VOYAGE 2 study were re-randomized to continue maintenance treatment with TREMFYA® 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® compared to placebo in both studies based on the Psoriasis Symptoms and Signs Diary (PSSD). Significantly greater proportions of patients on TREMFYA® 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 ≥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 ≥ 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 11: 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

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 12 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 12: Percent of Patients with ACR Responses[a,b] at Week 24 in DISCOVER 1 and DISCOVER 2

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

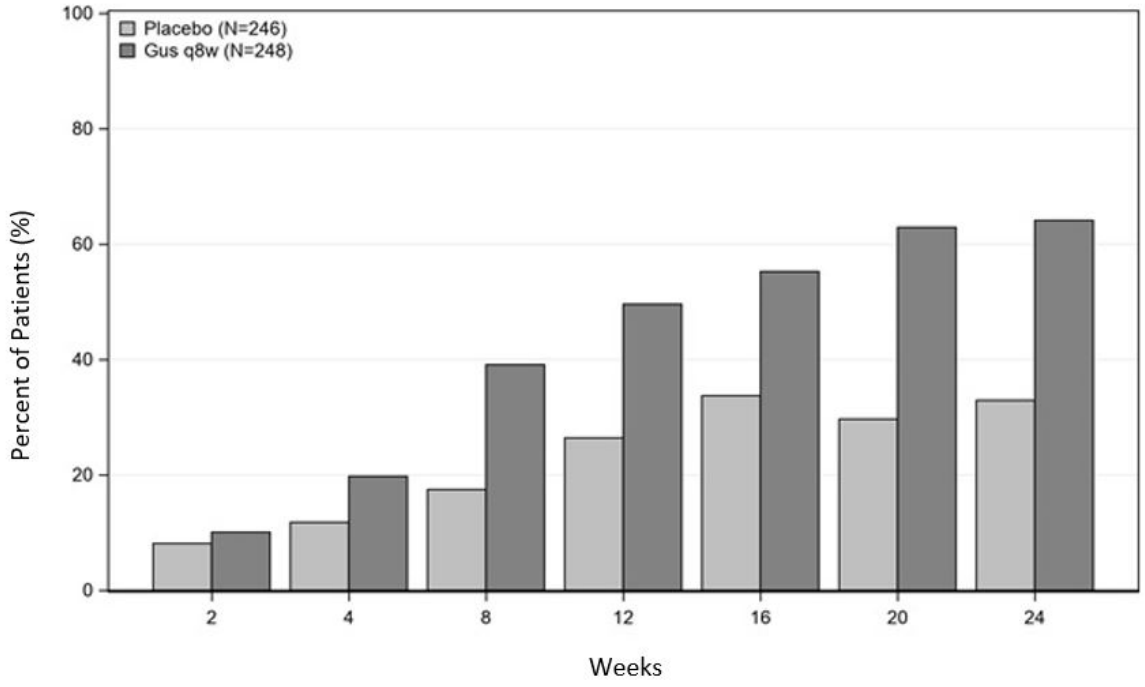
[a] Patients with <5% improvement from baseline in both tender and swollen joint counts at Week 16 were qualified for early escape and were permitted to initiate or increase the dose of concomitant medications including NSAIDs, oral corticosteroid and cDMARD, and remained on the randomized study treatment. 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® 100mg q8w groups respectively met early escape criteria.

[b] 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® 100 mg q8w group met treatment failure criteria.

[c] Treatment differences, 95% CIs and p-values were based on the Cochran-Mantel-Haenszel test stratified by baseline non-biologic cDMARD and prior anti-TNFα agents.

[d] 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, ≥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 13: 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)
No. of Swollen Joints				
Baseline	10.1	10.9	12.3	11.7
Mean change at Week 24	-5.1	-7.3	-6.4	-8.1
No. of Tender Joints				
Baseline	19.8	20.2	21.6	19.8
Mean change at Week 24	-6.8	-10.5	-7.3	-10.4
Patient's Assessment of Pain				
Baseline	5.8	6.0	6.3	6.3
Mean change at Week 24	-0.7	-2.2	-1.1	-2.5
Patient Global Assessment				
Baseline	6.1	6.5	6.5	6.5
Mean change at Week 24	-0.9	-2.5	-1.2	-2.5
Physician Global Assessment				
Baseline	6.3	6.2	6.7	6.6
Mean change at Week 24	-2.2	-3.5	-2.5	-3.8
Disability Index (HAQ-DI)				
Baseline	1.2	1.2	1.3	1.3
Mean change at Week 24	-0.1	-0.3	-0.2	-0.4
CRP (mg/dL)				
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.

Crohn's Disease

Table 14: Summary of trial designs and patient demographics

Study #	Trial design	Dosage, route of administration and duration	Total number of subjects	Mean age (Range)	Sex
GALAXI 2	A phase 3, multicentre, randomized, double-blind, placebo-controlled 48-week treat-through study	Guselkumab (n=146) 200 mg IV Weeks 0, 4, 8 → 200 mg SC q4w Guselkumab (n=143) 200 mg IV Weeks 0, 4, 8 → 100 mg SC q8w Placebo (n=76)	508	36.4 (18-74)	M=281 F=227
GALAXI 3	A phase 3, multicentre, randomized, double-blind, placebo-controlled 48-week treat-through study	Guselkumab (n=150) 200 mg IV Weeks 0, 4, 8 → 200 mg SC q4w Guselkumab (n=143) 200 mg IV Weeks 0, 4, 8 → 100 mg SC q8w Placebo (n=72)	513	36.6 (18-76)	M=307 F=206

GRAVITI	A phase 3, multicentre, randomized, double-blind, placebo-controlled 24-week treat-through study	Guselkumab (n=115) 400 mg SC Weeks 0, 4, 8 → 200 mg SC q4w Guselkumab (n=115) 400 mg SC Weeks 0, 4, 8 → 100 mg SC q8w Placebo (n=117)	347	37.5 (18-83)	M=203 F=144

The efficacy and safety of TREMFYA®/TREMFYA® I.V. were evaluated in three Phase 3 trials in adult patients with moderately to severely active Crohn's disease who had prior treatment failure (inadequate response, loss of response or intolerance) with either oral corticosteroids, conventional immunomodulators (AZA, 6-MP, MTX), and/or biologic therapy (TNF blocker or vedolizumab): two identically designed 48-week multicentre, randomized, double-blind, placebo- and biologic active-controlled, parallel group trials (intravenous induction and subcutaneous (SC) maintenance: GALAXI 2 and GALAXI 3) and one 48-week multicentre, randomized, double-blind, placebo-controlled, parallel group trial (SC induction and SC maintenance: GRAVITI). Moderately to severely active Crohn's disease was defined as a Crohn's Disease Activity Index (CDAI) score of ≥ 220 and ≤ 450 and a Simple Endoscopic Score for CD (SES-CD) of ≥6 (or ≥4 for patients with isolated ileal disease). In addition, efficacy and safety of TREMFYA®/TREMFYA® I.V. were evaluated in a Phase 2 dose-ranging study (GALAXI 1). All four trials had a treat-through study design: patients randomized to TREMFYA®/TREMFYA® I.V. maintained that treatment assignment for the duration of the trial.

IV Induction / SC Maintenance Studies: GALAXI 2 and GALAXI 3

Patients were randomized in a 2:2:2:1 ratio to receive TREMFYA® I.V. 200 mg induction at Weeks 0, 4 and 8 followed by TREMFYA® 200 mg SC maintenance every 4 weeks (q4w) (n = 146 in GALAXI 2 and n = 150 in GALAXI 3); or TREMFYA® I.V. 200 mg induction at Weeks 0, 4 and 8, followed by TREMFYA® 100 mg SC maintenance every 8 weeks (q8w) (n = 143 in both GALAXI 2 and GALAXI 3); or ustekinumab 6 mg/kg IV induction at Week 0 followed by ustekinumab 90 mg SC q8w maintenance (n = 143 in GALAXI 2 and n = 148 in GALAXI 3); or placebo (n = 76 in GALAXI 2 and n = 72 in GALAXI 3). Placebo non-responders received ustekinumab starting at Week 12. Randomization (see Table 14) was stratified by baseline CDAI score (≤300 or >300), baseline SES-CD score (≤12 or >12), prior BIO-Failure status (Yes/No) and baseline corticosteroid use (Yes/No).

A total of 1021 patients were evaluated in GALAXI 2 (N=508) and GALAXI 3 (N=513). The median age was 34 years; 42.4% were female; and 74.3% identified as White, 21.3% as Asian, and 1.5% as Black or African American.

In GALAXI 2, 52.8% of patients had previously failed at least one biologic therapy, 41.9% were biologic-naïve, and 5.3% had previously received but had not failed a biologic. At baseline, 37.4% of patients were receiving oral corticosteroids and 29.9% of patients were receiving conventional immunomodulators. The median CDAI score was 284.5 and the median SES-CD score was 11.0.

In GALAXI 3, 51.9% of patients had previously failed at least one biologic therapy, 41.5% were biologic-naïve, and 6.6% had previously received but had not failed a biologic. At baseline, 36.1% of patients were receiving oral corticosteroids and 30.2% of patients were receiving

conventional immunomodulators. The median CDAI score was 286 and the median SES-CD score was 11.0.

In GALAXI 2 and GALAXI 3, the composite co-primary endpoints were (1) clinical response at Week 12 and clinical remission at Week 48 and (2) clinical response at Week 12 and endoscopic response at Week 48 compared to placebo (Table 15). Key secondary composite endpoints included clinical response at Week 12 and corticosteroid-free clinical remission at Week 48, and clinical response at Week 12 and endoscopic remission at Week 48.

Clinical response is defined as ≥100-point reduction from baseline in CDAI score or CDAI score <150. Clinical remission is defined as a CDAI score <150. Endoscopic response is defined as ≥ 50% improvement (reduction) from baseline in SES-CD Score or SES-CD Score ≤ 2. Endoscopic remission is defined as a SES-CD Score ≤ 4 and at least a 2-point reduction from baseline with no subscore greater than 1 in any individual component. For composite endpoints, the same subject had to achieve each component of the endpoint.

The findings for primary and key secondary endpoints are shown in Table 15.

Table 15: Primary and Key Secondary Composite Endpoints in GALAXI 2 and GALAXI 3

GALAXI 2					
Endpoint	**Placebo N=76**	**TREMFYA® I.V. Induction → 100 mg SC q8w[a] N=143**	**TREMFYA® I.V. Induction → 200 mg SC q4w[b] N=146**	**Treatment Difference (95% CI)[c]**	
				TREMFYA® 100 mg	**TREMFYA® 200 mg**
Co-primary endpoints					
Clinical response at Week 12 and clinical remission at Week 48	9 (12%)	70 (49%)	80 (55%)	38% (27%, 49%)[d]	43% (32%, 54%)[d]
Clinical response at Week 12 and endoscopic response at Week 48	4 (5%)	56 (39%)	56 (38%)	34% (24%, 43%)[d]	33% (24%, 42%)[d]
Key secondary endpoints					
Clinical response at Week 12 and corticosteroid-free clinical remission at Week 48	7 (9%)	67 (47%)	74 (51%)	39% (28%, 49%)[d]	41% (31%, 52%)[d]
Clinical response at Week 12 and endoscopic remission at Week 48	2 (3%)	38 (27%)	48 (33%)	24% (16%, 32%)[d]	30% (21%, 39%)[d]
GALAXI 3					
Endpoint	**Placebo (N=72)**	**TREMFYA® I.V. Induction → 100 mg SC q8w[a] (N=143)**	**TREMFYA® I.V. Induction → 200 mg SC q4w[b] (N=150)**	**Treatment Difference (95% CI)[c]**	
				TREMFYA® 100 mg	**TREMFYA® 200 mg**
Co-primary endpoints					
Clinical response at Week 12 and clinical remission at Week 48	9 (13%)	67 (47%)	72 (48%)	34% (23%, 45%)[d]	35% (24%, 46%)[d]
Clinical response at Week 12 and endoscopic response at Week 48	4 (6%)	48 (34%)	54 (36%)	28% (19%, 37%)[d]	31% (21%, 40%)[d]
Key secondary endpoints					
Clinical response at Week 12 and corticosteroid-free clinical remission at Week 48	9 (13%)	65 (45%)	67 (45%)	33% (22%, 44%)[d]	31% (20%, 43%)[d]
Clinical response at Week 12 and endoscopic remission at Week 48	4 (6%)	34 (24%)	34 (23%)	18% (10%, 27%)[d]	17% (8%, 25%)[d]

[a] TREMFYA® I.V. 200 mg at Weeks 0, 4, and 8 followed by TREMFYA® 100 mg SC q8w.

[b] TREMFYA® I.V. 200 mg at Weeks 0, 4, and 8 followed by TREMFYA® 200 mg SC q4w.

[c] The adjusted treatment difference and the CIs were based on the common risk difference test using Mantel-Haenszel stratum weights and the Sato variance estimator.

[d] Statistically significant versus placebo based on the pre-defined testing hierarchy at the 2-sided 0.05 significance level

In GALAXI 2, in subjects who had prior biologic failure receiving TREMFYA® I.V. followed by TREMFYA® 100 mg SC q8w / TREMFYA® 200 mg SC q4w (N=77/N=73), 39%/52% demonstrated clinical response at Week 12 and clinical remission at Week 48, and 36%/26% demonstrated clinical response at Week 12 and endoscopic response at Week 48, compared with 13% and 5%, respectively, in subjects receiving placebo (N=39). In subjects who were

biologic-naïve receiving TREMFYA® I.V. followed by TREMFYA® 100 mg SC q8w / TREMFYA® 200 mg SC q4w (N=58/N=63), 60%/59% demonstrated clinical response at Week 12 and clinical remission at Week 48, and 45%/49% demonstrated clinical response at Week 12 and endoscopic response at Week 48, compared with 9% and 6%, respectively, in subjects receiving placebo (N=34).

In GALAXI 3, in subjects who had prior biologic failure receiving TREMFYA® I.V. followed by TREMFYA® 100 mg SC q8w / TREMFYA® 200 mg SC q4w (N=76/N=74), 53%/47% demonstrated clinical response at Week 12 and clinical remission at Week 48, and 36%/36% demonstrated clinical response at Week 12 and endoscopic response at Week 48, compared with 13% and 5%, respectively, in subjects receiving placebo (N=39). In subjects who were biologic-naïve receiving TREMFYA® I.V. followed by TREMFYA® 100 mg SC q8w / TREMFYA® 200 mg SC q4w (N=58/N=65), 43%/51% demonstrated clinical response at Week 12 and clinical remission at Week 48, and 36%/38% demonstrated clinical response at Week 12 and endoscopic response at Week 48, compared with 15% and 7%, respectively, in subjects receiving placebo (N=27).

In GALAXI 2, following the induction period, 47% (n=136) of subjects receiving TREMFYA® I.V. demonstrated clinical remission at Week 12 and 38% (n=109) demonstrated endoscopic response at Week 12, compared with 22% (n=17) and 11% (n=8), respectively, of subjects receiving placebo. In GALAXI 3, following the induction period, 47% (n=138) of subjects receiving TREMFYA® I.V. demonstrated clinical remission at Week 12 and 36% (n=106) demonstrated endoscopic response at Week 12, compared with 15% (n=11) and 14% (n=10), respectively, of subjects receiving placebo.

SC Induction / SC Maintenance Study: GRAVITI

In GRAVITI, patients were randomized in a 1:1:1 ratio to receive TREMFYA® 400 mg SC induction at Weeks 0, 4 and 8 followed by TREMFYA® 200 mg SC q4w maintenance (n = 115); or TREMFYA® 400 mg SC induction at Weeks 0, 4 and 8, followed by TREMFYA® 100 mg SC q8w maintenance (n = 115); or placebo (n = 117). All patients in the placebo group who met rescue criteria received treatment with TREMFYA® 400 mg SC induction followed by TREMFYA® 100 mg SC maintenance every 8 weeks. The randomization (see Table 14) was stratified by baseline CDAI score (≤300 or >300), baseline SES-CD score (≤12 or >12), and prior BIO-Failure status (Yes/No).

A total of 347 patients were evaluated. The median age of patients was 36 years; 41.5% were female; and 66% identified as White, 21.9% as Asian, and 2.6% as Black or African American.

In GRAVITI, 46.4% of patients had previously failed at least one biologic therapy, 46.4% were biologic-naïve, and 7.2% had previously received but had not failed a biologic. At baseline, 29.7% of patients were receiving oral corticosteroids and 28.5% of the patients were receiving conventional immunomodulators. The median CDAI score was 289 and the median SES-CD score was 10.0.

The co-primary endpoints were clinical remission at Week 12 and endoscopic response at Week 12 compared to placebo (Table 16).

The results at week 12 following the induction period are shown in Table 16.

Table 16: Efficacy Endpoints at Week 12 in GRAVITI

Endpoint	Placebo (N=117)	TREMFYA® 400 mg SC[a] (N=230)	Treatment Difference vs Placebo (95% CI)[b]
Clinical Remission at Week 12	25 (21%)	129 (56%)	35% (25%, 45%)[c]
Endoscopic Response at Week 12	25 (21%)	95 (41%)	20% (10%, 30%)[c]

[a] TREMFYA® 400 mg SC induction at Weeks 0, 4 and 8

[b] The adjusted treatment difference and the CIs were based on the common risk difference test using Mantel-Haenszel stratum weights and the Sato variance estimator.

[c] Statistically significant versus placebo based on the pre-defined testing hierarchy at the 2-sided 0.05 significance level

In GRAVITI, in subjects who had prior biologic failure receiving TREMFYA® 400 mg SC (N=108), 60% demonstrated clinical remission at Week 12 and 33% demonstrated endoscopic response at Week 12, compared with 17% and 17%, respectively, in subjects receiving placebo (N=53). In subjects receiving TREMFYA® 400 mg SC who were biologic-naïve (N=105), 50% demonstrated clinical remission at Week 12 and 49% demonstrated endoscopic response at Week 12, compared with 25% and 27%, respectively, in subjects receiving placebo (N=56).

In GRAVITI, following the maintenance period, the endpoints of clinical remission, endoscopic response, and endoscopic remission at week 48 were consistent with the maintenance results observed in the GALAXI 2/GALAXI 3 studies.

Ulcerative Colitis

Table 17: Summary of trial designs and patient demographics

Study #	Trial design	Dosage, route of administration and duration	Total number of subjects	Mean age (Range)	Gender
QUASAR induction dose-ranging study	A phase 2b, multicenter, randomized, double-blind, placebo-controlled study	Guselkumab (n=107) 400 mg IV Weeks 0, 4, 8 Guselkumab (n=101) 200 mg IV Weeks 0, 4, 8 Placebo (n=105) IV	313	39 (18-84)	M=185 F=128
QUASAR-IS	A phase 3, multicenter, randomized, double-blind, placebo-controlled study	Guselkumab (n=421) 200 mg IV Weeks 0, 4, 8 Placebo (n=280) IV	701	39 (18-79)	M=399 F=302

QUASAR-M	A phase 3, multicenter, randomized, double-blind, placebo-controlled study	Guselkumab (n=190) 200 mg SC every 4 weeks Guselkumab (n=188) 100 mg SC every 8 weeks Placebo (n=190) SC	568	39 (18-79)	M=311 F=257

The efficacy and safety of TREMFYA®/TREMFYA® I.V. were evaluated in two Phase 3 multicenter, randomized, double-blind, placebo-controlled studies (QUASAR induction study and QUASAR maintenance study) in adult patients with moderately to severely active ulcerative colitis who had an inadequate response, loss of response, or intolerance to corticosteroids, conventional immunomodulators, and/or an advanced therapy (biologic therapy [TNF blockers, vedolizumab], or a Janus kinase [JAK] inhibitor). In addition, efficacy and safety of TREMFYA® I.V. were evaluated in a randomized, double-blind, placebo controlled, Phase 2b induction dose-finding study (QUASAR induction dose-ranging study).

Disease activity was assessed by the modified Mayo score (mMS), a 3-component Mayo score (0-9) which consists of the sum of the following subscores (0 to 3 for each subscore): stool frequency (SFS), rectal bleeding (RBS), and findings on centrally reviewed endoscopy (ES). Moderately to severely active ulcerative colitis was defined as a mMS between 5 and 9, an RBS $\geq$1, and an ES of 2 (defined by marked erythema, absent vascular pattern, friability, and/or erosions) or an ES of 3 (defined by spontaneous bleeding and ulceration).

QUASAR Induction Study: QUASAR IS

In the induction study QUASAR IS, a total of 701 subjects were randomized in a 3:2 ratio to receive either TREMFYA® I.V. 200 mg (n = 421) or placebo by intravenous infusion at Week 0, Week 4, and Week 8 (n = 280). Randomization was stratified by ADT-failure status (ie, inadequate response or failure to tolerate TNFα antagonists, vedolizumab, or tofacitinib) (Yes/No), region (Eastern Europe, Asia, or Rest of World), and concomitant use of corticosteroids at baseline (Yes/No) (see Table 17).

At baseline the median mMS was 7, with 35.5% of patients having a baseline mMS of 5 to 6 and 64.5% having a mMS of 7 to 9, and 67.9% of patients with a baseline ES of 3. Extensive disease was present in 47.8% of subjects. The median age was 39 years (ranging from 18 to 79 years); 43.1% were female; and 72.5% identified as White, 21.4% as Asian, 1% as Black, 0.1% as American Indian or Alaskan Native, and 0.1% as multiple racial groups.

Enrolled subjects were permitted to use stable doses of oral aminosalicylates, methotrexate, 6-MP, AZA and/or oral corticosteroids. At baseline, 72.5% of subjects were receiving aminosalicylates, 20.8% of subjects were receiving immunomodulators (MTX, 6-MP, or AZA), and 43.1% of subjects were receiving corticosteroids. Concomitant biologic therapies or JAK inhibitors were not permitted.

A total of 49.1% of subjects had previously failed at least one advanced therapy. Of these subjects, 87.5%, 54.1% and 18.0% had previously failed a TNF blocker, vedolizumab or a JAK inhibitor, respectively, and 47.4% had failed treatment with 2 or more of these therapies. A total

of 48.4% of subjects were advanced therapy naive, and 2.6% had previously received but had not failed an advanced therapy.

The primary endpoint was clinical remission as defined by the mMS at Week 12. Secondary endpoints at Week 12 included but were not limited to endoscopic improvement, clinical response, and histologic endoscopic mucosal improvement (see Table 18). Clinical remission is defined as a stool frequency subscore of 0 or 1 and not increased from induction baseline, a rectal bleeding subscore of 0, and an endoscopy subscore of 0 or 1 with no friability present on the endoscopy. Endoscopic improvement is defined as an endoscopy subscore of 0 or 1 with no friability present on the endoscopy. Clinical response is defined as a decrease from induction baseline in the modified Mayo score by ≥30% and ≥2 points, with either a ≥1-point decrease from induction baseline in the rectal bleeding subscore or a rectal bleeding subscore of 0 or 1. Histologic endoscopic mucosal improvement is defined as a combination of histologic improvement (neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations or granulation tissue according to the Geboes grading system) and endoscopic improvement as defined above.

The findings for the primary and key secondary endpoints assessed at Week 12 of QUASAR IS are shown in Table 18.

Table 18: Proportion of Patients Meeting Efficacy Endpoints at Week 12 in QUASAR IS

Endpoint	Placebo (N=280)	TREMFYA® I.V. 200 mg[a] (N=421)	Treatment Difference (95% CI)
Clinical remission	22 (8%)	95 (23%)	15% (10%, 20%)[b]
Advanced therapy naïve[c]	16/137 (12%)	64/202 (32%)	
Prior advanced therapy failure	5/136 (4%)	26/208 (13%)	
Endoscopic improvement	31 (11%)	113 (27%)	16% (10%, 21%)[b]
Advanced therapy naïve[c]	23/137 (17%)	77/202 (38%)	
Prior advanced therapy failure	7/136 (5%)	31/208 (15%)	
Clinical response	78 (28%)	259 (62%)	34% (27%, 41%)[b]
Advanced therapy naïve[c]	48/137 (35%)	144/202 (71%)	
Prior advanced therapy failure	27/136 (20%)	107/208 (51%)	
Histologic endoscopic mucosal improvement	21 (8%)	99 (24%)	16% (11%, 21%)[b]
Advanced therapy naïve[c]	15/137 (11%)	66/202 (33%)	
Prior advanced therapy failure	6/136 (4%)	28/208 (13%)	

[a] TREMFYA® I.V. 200 mg as an intravenous infusion at Week 0, Week 4, and Week 8.

[b] Statistically significant versus placebo based on the pre-defined testing hierarchy at the 2-sided 0.05 significance level, adjusted treatment difference (95% CI) based on Cochran-Mantel-Haenszel method (adjusted for stratification factors: advanced therapy failure status and concomitant use of corticosteroids at baseline).

[c] Does not include an additional 7 participants in the placebo group and 11 participants in the TREMFYA® group who were previously exposed to but did not fail an advanced therapy.

Symptomatic Assessment
Symptomatic remission is defined as a stool frequency subscore of 0 or 1 and not increased from induction baseline, and a rectal bleeding subscore of 0. At Week 12, symptomatic remission was achieved in 50% of subjects treated with TREMFYA® I.V. and 21% of subjects treated with placebo. At Week 4, symptomatic remission was achieved in 23% of subjects treated with TREMFYA® I.V. and 13% of subjects treated with placebo.

Endoscopic Assessment
Endoscopic remission (endoscopy subscore of 0) at Week 12 was achieved in 15% of subjects treated with TREMFYA® I.V. and 5% of subjects treated with placebo.

Health Related Quality of Life
Fatigue response is defined as a ≥7 point improvement from baseline, which is considered clinically meaningful, as assessed using the PROMIS-Fatigue Short form 7a. At Week 12, fatigue response was achieved in 41% of subjects treated with TREMFYA® I.V. and 21% of subjects treated with placebo.

IBDQ remission (Total Inflammatory Bowel Disease Questionnaire score ≥170) at Week 12 was achieved in 51% of subjects treated with TREMFYA® I.V. and 30% of subjects treated with placebo.

Maintenance Study: QUASAR MS
The maintenance study (QUASAR MS) evaluated 568 subjects who achieved clinical response at Week 12 following the intravenous administration of TREMFYA® I.V. in either QUASAR IS or from the QUASAR induction dose-ranging study. These subjects were randomized in a 1:1:1 ratio to receive a subcutaneous maintenance regimen of either TREMFYA® 100 mg every 8 weeks, TREMFYA® 200 mg every 4 weeks or placebo for 44 weeks. Randomization was stratified by clinical remission status at maintenance baseline (Yes/No), concomitant use of corticosteroids at maintenance baseline (Yes/No), and induction treatment (TREMFYA® I.V. 400 mg, TREMFYA® I.V. 200 mg, and placebo IV → TREMFYA® I.V. 200 mg) (see Table 17).

The primary endpoint was clinical remission as defined by mMS at Week 44. Secondary endpoints at Week 44 included but were not limited to symptomatic remission, endoscopic improvement, corticosteroid-free clinical remission, histologic endoscopic mucosal improvement, and fatigue response (see Table 19). Clinical remission is defined as a stool frequency subscore of 0 or 1 and not increased from induction baseline, a rectal bleeding subscore of 0, and an endoscopy subscore of 0 or 1 with no friability present on the endoscopy. Endoscopic improvement is defined as an endoscopy subscore of 0 or 1 with no friability present on the endoscopy. Clinical response is defined as a decrease from induction baseline in the modified Mayo score by ≥30% and ≥2 points, with either a ≥1-point decrease from induction baseline in the rectal bleeding subscore or a rectal bleeding subscore of 0 or 1. Histologic endoscopic mucosal improvement is defined as a combination of histologic improvement (neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations or

granulation tissue according to the Geboes grading system) and endoscopic improvement as defined above.

The findings for the primary and key secondary endpoints assessed at Week 44 of QUASAR MS are shown in Table 19.

Table 19: Proportion of Subjects Meeting Efficacy Endpoints at Week 44 in QUASAR MS

Endpoint	Placebo N=190	TREMFYA® 100 mg q8w[a] N=188	TREMFYA® 200 mg q4w[b] N=190	Treatment Difference vs Placebo (95% CI)	
				TREMFYA® 100 mg	TREMFYA® 200 mg
Clinical remission	36 (19%)	85 (45%)	95 (50%)	25% (16%, 34%)[c]	30% (21%, 38%)[c]
Advanced therapy naïve[d]	28/108 (26%)	53/105 (50%)	56/96 (58%)		
Prior advanced therapy failure	6/75 (8%)	31/77 (40%)	35/88 (40%)		
Corticosteroid-free clinical remission[e]	35 (18%)	85 (45%)	93 (49%)	26% (17%, 34%)[c]	29% (20%, 38%)[c]
Advanced therapy naïve[d]	28/108 (26%)	53/105 (50%)	54/96 (56%)		
Prior advanced therapy failure	5/75 (7%)	31/77 (40%)	35/88 (40%)		
Endoscopic improvement	36 (19%)	93 (49%)	98 (52%)	30% (21%, 38%)[c]	31% (22%, 40%)[c]
Advanced therapy naïve[d]	28/108 (26%)	56/105 (53%)	57/96 (59%)		
Prior advanced therapy failure	6/75 (8%)	35/77 (45%)	37/88 (42%)		
Histologic endoscopic mucosal improvement	32 (17%)	82 (44%)	91 (48%)	26% (17%, 34%)[c]	30% (21%, 38%)[c]
Advanced therapy naïve[d]	25/108 (23%)	52/105 (50%)	54/96 (56%)		
Prior advanced therapy failure	6/75 (8%)	29/77 (38%)	34/88 (39%)		
Clinical response	82 (43%)	146 (78%)	142 (75%)	34% (25%, 43%)[c]	31% (21%, 40%)[c]
Advanced therapy naïve[d]	58/108 (54%)	87/105 (83%)	78/96 (81%)		
Prior advanced therapy failure	21/75 (28%)	54/77 (70%)	59/88 (67%)		

[a] TREMFYA® 100 mg as a subcutaneous injection every 8 weeks after the induction regimen.

[b] TREMFYA® 200 mg as a subcutaneous injection every 4 weeks after the induction regimen.

[c] Statistically significant versus placebo based on the pre-defined testing hierarchy at the 2-sided 0.05 significance level, adjusted treatment difference (95% CI) based on Cochran-Mantel-Haenszel method adjusted for randomization stratification factors.

[d] Does not include an additional 7 participants in the placebo group, 6 participants in the TREMFYA® 100mg group, and 6 participants in the TREMFYA® 200mg group who were previously exposed to but did not fail an advanced therapy.

[e] Not requiring any treatment with corticosteroids for at least 8 weeks prior to Week 44 and also meeting the criteria for clinical remission at Week 44.

Symptomatic Assessment

Symptomatic remission is defined as a stool frequency subscore of 0 or 1 and not increased from induction baseline, and a rectal bleeding subscore of 0. At Week 44, symptomatic remission was achieved in 70% of subjects treated with TREMFYA® 100 mg q8w, 69% of subjects treated with TREMFYA® 200 mg q4w, and 37% of subjects treated with placebo.

Maintenance of Clinical Remission
Maintenance of clinical remission at Week 44 in subjects who achieved clinical remission 12 weeks after induction was achieved in 61% of subjects treated with TREMFYA® 100 mg q8w, 72% of subjects treated with TREMFYA® 200 mg q4w, and 34% of subjects treated with placebo.

Endoscopic and Histologic Assessment
Endoscopic remission (endoscopy subscore of 0) at Week 44 was achieved in 35% of subjects treated with TREMFYA® 100 mg q8w, 34% of subjects treated with TREMFYA® 200 mg q4w, and 15% of subjects treated with placebo.

Histologic remission (Geboes histologic score ≤2 B.0 indicating the absence of neutrophils from the mucosa [both lamina propria and epithelium], no crypt destruction, and no erosions, ulcerations or granulation tissue) at Week 44 was achieved by 59% subjects treated with TREMFYA® 100 mg SC q8w, 61% of subjects treated with TREMFYA® 200 mg SC q4w, and 27% of subjects treated with placebo.

Combined endoscopic remission and histologic remission at Week 44 was achieved by 31% of subjects treated with TREMFYA® 100 mg SC q8w, 33% of subjects treated with TREMFYA® 200 mg SC q4w, and 14% of subjects treated with placebo.

Health Related Quality of Life
Fatigue response is defined as a ≥7-point improvement from baseline, which is considered clinically meaningful, as assessed using the PROMIS-Fatigue Short form 7a. At Week 44, fatigue response was achieved in 51% of subjects treated with TREMFYA® 100 mg q8w, 43% of subjects treated with TREMFYA® 200 mg q4w, and 29% of subjects treated with placebo.

IBDQ remission (Total Inflammatory Bowel Disease Questionnaire score ≥170) at Week 44 was achieved in 64% of subjects treated with TREMFYA® 100 mg q8w, 64% of subjects treated with TREMFYA® 200 mg q4w, and 37% of subjects treated with placebo.

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 dose (50 mg/kg once weekly), AUC_{last} was approximately 23 times the clinical exposure following a dose of 200 mg given intravenously.

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 (AUC_{last} at the 10 mg/kg dose was 7-fold greater than human levels following a dose of 200 mg given subcutaneously). 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 (AUC_{last} was 21-fold greater than human levels following a dose of 200 mg given subcutaneously).

In a male fertility and early embryonic development toxicity study conducted in guinea pigs, the incidence of total litter loss increased in untreated females (5 of 22 untreated females) mated with males administered 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 (AUC_{last} was 10-fold greater than human levels following a dose of 200 mg given subcutaneously).

PATIENT MEDICATION INFORMATION (TREMFYA®)

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrTREMFYA®

(guselkumab injection)
Solution for injection

100 mg/1 mL pre-filled syringe
100 mg/1 mL TREMFYA One-Press® (patient-controlled injector)
200 mg/2 mL pre-filled syringe
200 mg/2 mL pen

Read this carefully before you start taking **TREMFYA®** 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®**.

What is TREMFYA® used for?

- **Plaque Psoriasis**

TREMFYA® 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® reduces the inflammation and other symptoms of the disease.

- **Psoriatic Arthritis**

TREMFYA® 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® alone or in combination with a conventional Disease Modifying Anti-Rheumatic Drug (cDMARD) such as methotrexate. TREMFYA® reduces signs and symptoms of your arthritis and may improve symptoms in patients that have psoriasis.

- **Crohn's Disease**

TREMFYA® is used to treat adults with moderately to severely active Crohn's disease, an inflammatory disease of the bowel. Using TREMFYA® in Crohn's disease can benefit you by reducing the signs and symptoms of the disease such as diarrhea, abdominal pain, and the inflammation of your intestinal lining. This may enable your normal daily activities and reduce fatigue.

- **Ulcerative Colitis**

TREMFYA® is used to treat adults with moderately to severely active ulcerative colitis, an inflammatory disease of the bowel. Using TREMFYA® in ulcerative colitis will benefit you by reducing the signs and symptoms of the disease including bloody stools, the need to rush to

and the number of times you go to the toilet, abdominal pain and the inflammation of your intestinal lining. This may enable your normal daily activities and reduce fatigue.

How does TREMFYA® work?

TREMFYA® 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, psoriatic arthritis, Crohn's disease and ulcerative colitis.

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

What are the ingredients in TREMFYA®?

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:

Pre-filled syringe:

- 100 mg in 1 mL of solution for injection in a single-dose pre-filled syringe
- 200 mg in 2 mL of solution for injection in a single-dose pre-filled syringe

Pen:

- 200 mg in 2 mL of solution for injection in a single-dose pre-filled pen

TREMFYA One-Press®:

- 100 mg in 1 mL of solution for injection in a single-dose patient-controlled injector

Do not use TREMFYA® if:

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

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

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take TREMFYA®. 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® 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®. You should not be given certain types of vaccines (live vaccines) while using TREMFYA®.
- 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® and for at least 12 weeks after the last TREMFYA® dose. Talk to your healthcare professional about your contraception options.
- are breast-feeding or plan to breast-feed. You and your healthcare professional should decide if you will breast-feed while using TREMFYA®.

Look out for infections and allergic reactions

- Do not use TREMFYA® if you have any symptoms of infection unless you are instructed by your healthcare provider.
- **After starting TREMFYA®, 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®. Tell your healthcare professional or seek medical help immediately if you experience these symptoms**.

Children and adolescents (below the age of 18 years)
TREMFYA® 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®:

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

TREMFYA® is given by injection under your skin (subcutaneous injection).

You and your healthcare professional should decide if you should inject TREMFYA® 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® injection after proper training.

Before use, take the carton out of the refrigerator and allow it to reach room temperature by waiting 30 minutes. Keep the TREMFYA® pre-filled syringe, pen, or TREMFYA One-Press® patient-controlled injector in the carton to protect from light.

Read the "Instructions for Use" document carefully before using TREMFYA®.

Usual dose:

Your healthcare professional will decide how much TREMFYA® you need and for how long.

Plaque Psoriasis

- The dose is 100 mg 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, followed by a dose every 8 weeks.

Psoriatic Arthritis

- The dose is 100 mg 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, followed by a dose every 8 weeks.

Crohn's Disease

Treatment start

Treatment start can be given by either intravenous infusion (drip in a vein in your arm) or administered subcutaneously (injections under the skin).

Intravenous Infusion (TREMFYA® I.V.):

- The first dose is 200 mg and will be given by your healthcare provider by intravenous infusion over at least 1 hour (refer to the Patient Medication Information for TREMFYA® I.V.).
- After the first dose, you will have the second dose by intravenous infusion 4 weeks later, and then a third dose by intravenous infusion after an additional 4 weeks.

Subcutaneous administration (TREMFYA®):

- The first dose is 400 mg and will be given by injections under the skin at different locations of the body.
- After the first dose, you will have a second 400 mg dose 4 weeks later and then a third 400 mg dose after an additional 4 weeks.

Maintenance therapy (TREMFYA®)

A maintenance dose will be given by injection under the skin (subcutaneous injection) either with 100 mg or 200 mg. Your healthcare provider will decide which maintenance dose you will receive:

- A dose of 100 mg will be given 8 weeks after the third treatment start dose, followed by a dose every 8 weeks.
- A dose of 200 mg will be given 4 weeks after the third treatment start dose, followed by a dose every 4 weeks.

Ulcerative Colitis

Treatment start (TREMFYA® I.V.)

- The first dose is 200 mg and will be given by your healthcare provider by intravenous infusion (drip in a vein in your arm) over at least 1 hour (refer to the Patient Medication Information for TREMFYA® I.V.).
- After the first dose, you will have the second dose by intravenous infusion 4 weeks later, and then a third dose by intravenous infusion after an additional 4 weeks.

Maintenance therapy (TREMFYA®)

A maintenance dose will be given by injection under the skin (subcutaneous injection) either with 100 mg or 200 mg. Your healthcare provider will decide which maintenance dose you will receive:

- A dose of 100 mg will be given 8 weeks after the third treatment start dose, followed by a dose every 8 weeks.
- A dose of 200 mg will be given 4 weeks after the third treatment start dose, followed by a dose every 4 weeks.

TREMFYA® 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® unless you think it is causing a severe side effect. Speak to your healthcare professional as soon as possible if this happens.

Overdose:

If you accidentally inject more TREMFYA® 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®, 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® 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®?

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®. 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® in the refrigerator between 2°C to 8°C (36°F to 46°F).

Do not freeze. Do not use if TREMFYA® has been frozen.

Do not shake TREMFYA®.

Store in original packaging to protect from light until use.

Keep out of reach and sight of children.

Do not use TREMFYA®:

- 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® is for single use only. Ask your healthcare professional how to throw away medicines that are no longer required.

If you want more information about TREMFYA®:

- Talk to your healthcare professional
- For questions or concerns, contact the manufacturer, Janssen Inc. (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://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website 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.

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INSTRUCTIONS FOR USE (TREMFYA® 100 mg Pre-filled Syringe)

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 healthcare professional 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 healthcare professional about your medical condition or your treatment. Please also read the Package Insert carefully and discuss any questions you may have with your healthcare professional.
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.

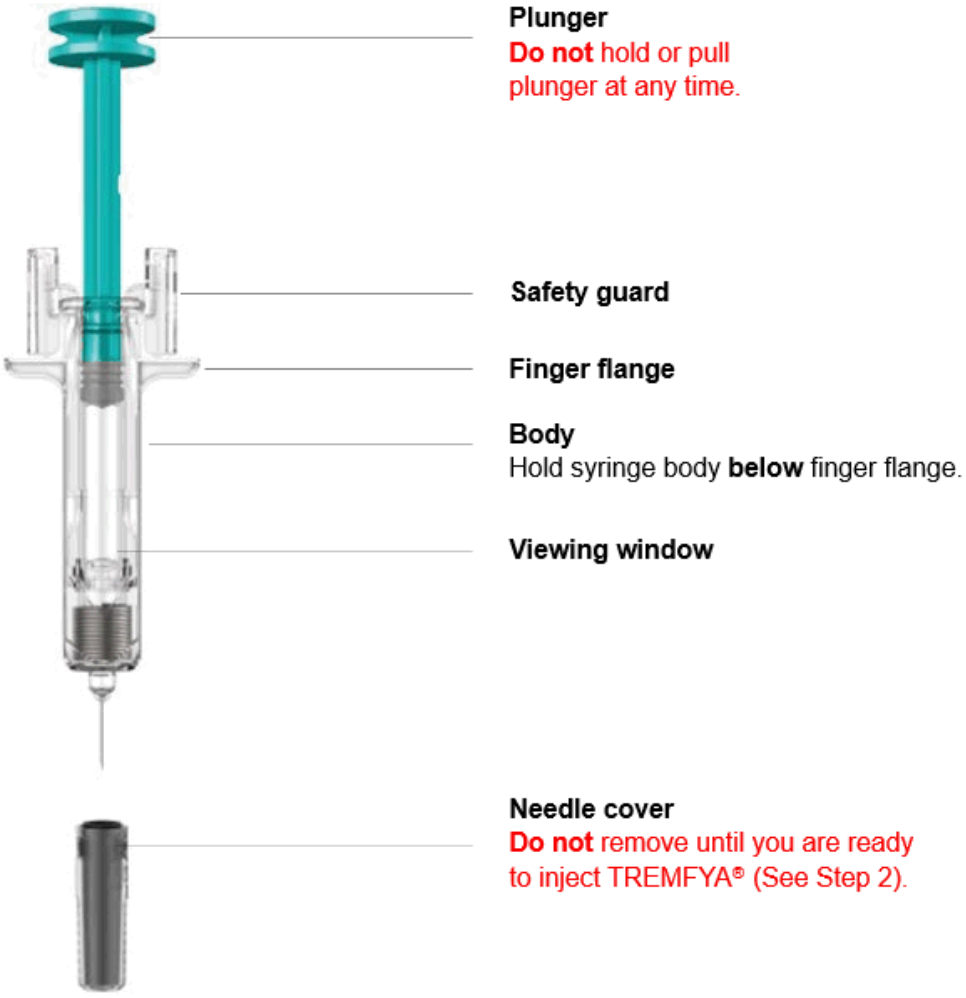
Keep TREMFYA® and all medicines out of reach and sight of children.

Do not shake the pre-filled syringe.

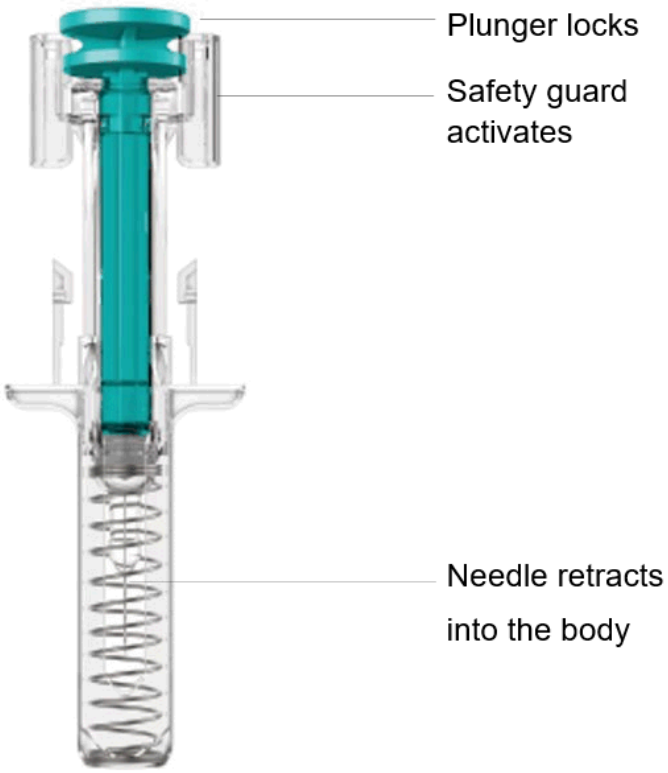
Keep TREMFYA® pre-filled syringe in the original carton to protect from light and physical damage.

Pre-filled syringe parts

Before injection



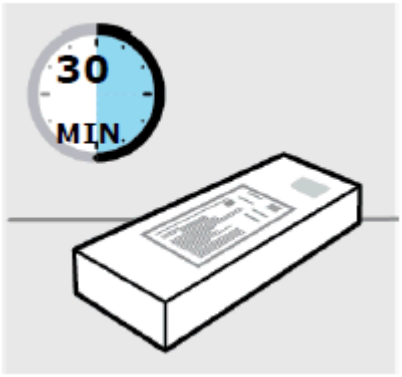
After injection



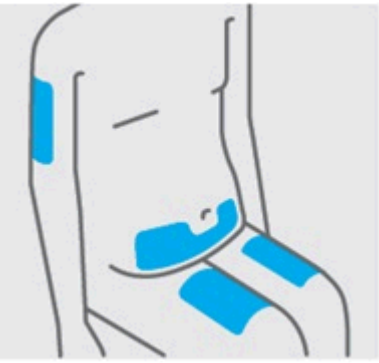
You will need these additional supplies:

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

1. Prepare for your injection

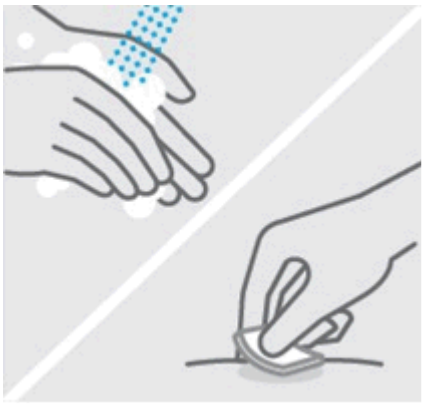


Inspect carton
Remove carton with the pre-filled syringe from the refrigerator.
Keep the pre-filled syringe in the carton and let it sit on a flat surface at room temperature for **at least 30 minutes** before use.
Do not warm any other way.
Check the expiration date ('EXP') on the back panel of the carton.
DO NOT use if the expiration date has passed.
Do not inject TREMFYA® if the perforations on the carton are broken.
Call your healthcare professional for a refill.

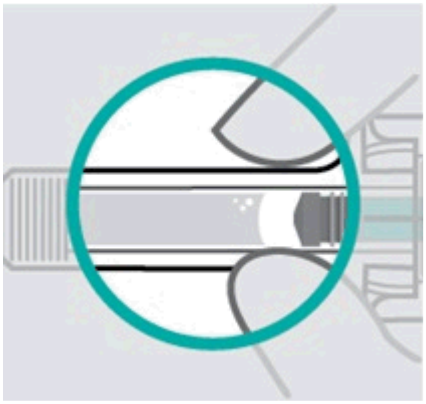


Choose injection site
Select from the following areas for your injection:
- **Front of thighs** (recommended)
- Lower abdomen
  Do not use the 2-inch (5-centimetre) area around belly-button.
- Back of upper arms (if a caregiver is giving you the injection)

DO NOT inject into skin that is tender, bruised, red, scaly or hard.
Do not inject into areas with scars or stretch marks.

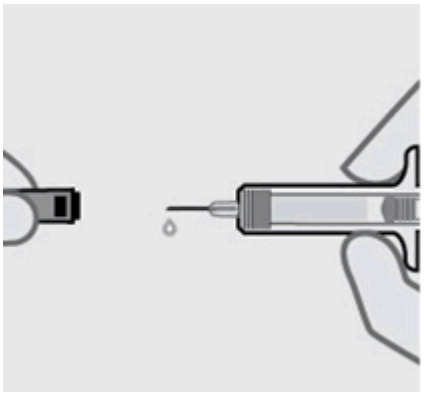


Clean injection site
Wash your hands well with soap and warm water.
Wipe your chosen injection site with an alcohol swab and allow it to dry.
Do not touch, fan or blow on the injection site after you have cleaned it.

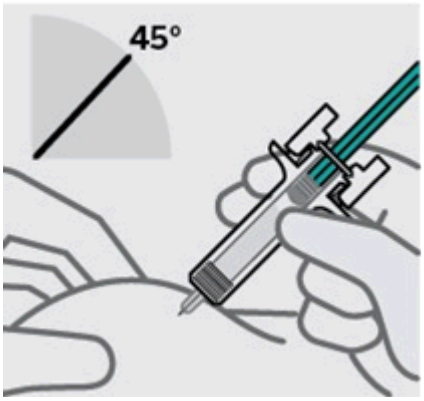


Inspect liquid
Take the pre-filled syringe out of the carton.
Check the liquid in the viewing window. It should be clear to slightly yellow and may contain tiny white or clear particles. You may also see one or more air bubbles.
This is normal.
Do not inject if the liquid is cloudy or discolored, or has large particles. Call your healthcare professional for a refill.

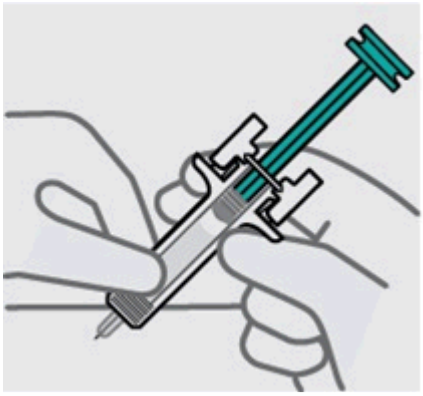
2. Inject TREMFYA® using the pre-filled syringe



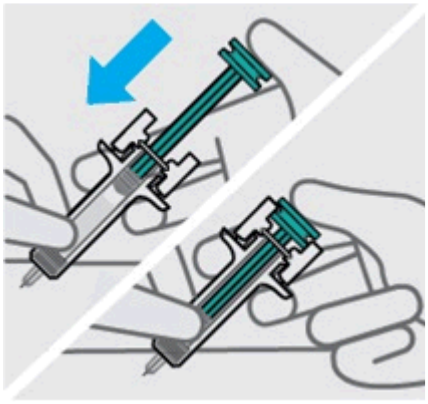
Remove needle cover
Hold syringe by the body and pull needle cover straight off.
It is normal to see a drop of liquid.
Inject within 5 minutes of removing the needle cover.
DO NOT put needle cover back on, as this may damage the needle or cause a needle stick injury.
DO NOT touch needle or let it touch any surface.
DO NOT use the TREMFYA® pre-filled syringe if it is dropped. Call your healthcare professional for a refill.



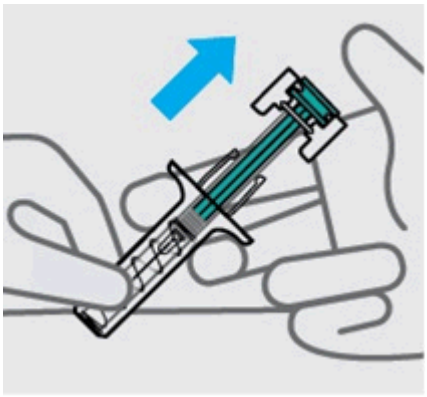
Position fingers and insert needle
Place your thumb, index and middle fingers **directly under the finger flange**, as shown.
Do not touch plunger or area above finger flange as this may cause the needle safety device to activate.
Use your other hand to pinch skin at the injection site.
Position syringe 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.



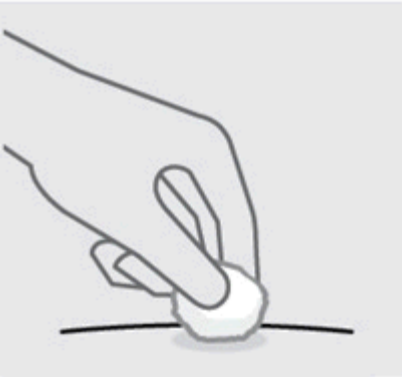
Press plunger
Place thumb from the opposite hand on the plunger and press the plunger **all the way down until it stops**.



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 healthcare professional 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 healthcare professional to talk about any questions you may have. For questions or concerns visit the manufacturer's website www.janssen.com/canada, or call 1-800-567-3331 or 1-800-387-8781.

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INSTRUCTIONS FOR USE (TREMFYA® 200 mg Pre-filled Syringe)

PrTREMFYA®
(guselkumab injection)

200 mg Pre-filled syringe

SINGLE-USE

PLEASE READ THESE INSTRUCTIONS BEFORE USE

Important

TREMFYA® comes in a single-use pre-filled syringe containing one 200 mg dose.

Your healthcare professional will tell you if you will need to use 1 or 2 pre-filled syringes.

If your healthcare professional 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.

Please read these Instructions for Use 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 healthcare professional 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 healthcare professional.

Each TREMFYA® pre-filled syringe can only be used one time. Throw the used pre-filled syringe away (see Step 4) after one dose, even if there is still medicine left in it. Do not reuse your TREMFYA® pre-filled syringe.

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 device and lock into place.

Storage information

Store in refrigerator at 2° to 8°C.
Do not freeze.
Do not shake your pre-filled syringe.
Keep your pre-filled syringe in the original carton to protect from light and physical damage.
Keep TREMFYA® and all medicines out of reach of children.

Pre-filled syringe at-a-glance

Before use

Plunger

Do not hold or pull plunger at any time.

Safety guard

Finger flange

Viewing window

Body

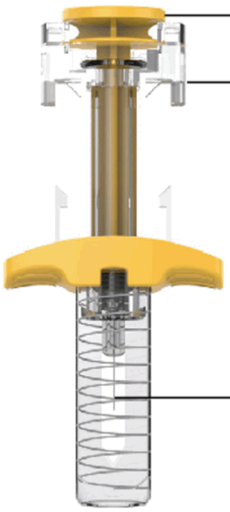
Needle

Needle cover

Do not remove until you are ready to inject

(See Step 3)

After use



Plunger locks

Safety guard activates

Needle retracts into the body

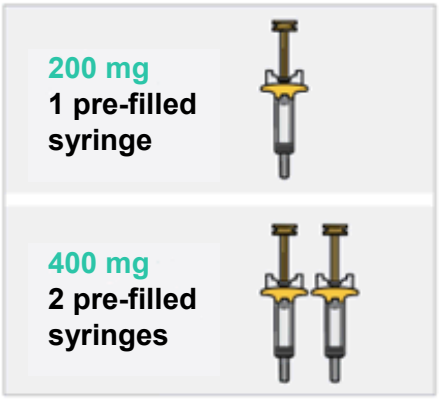
You will need:

- **1 or 2 pre-filled syringes based on the dose prescribed by your healthcare professional**

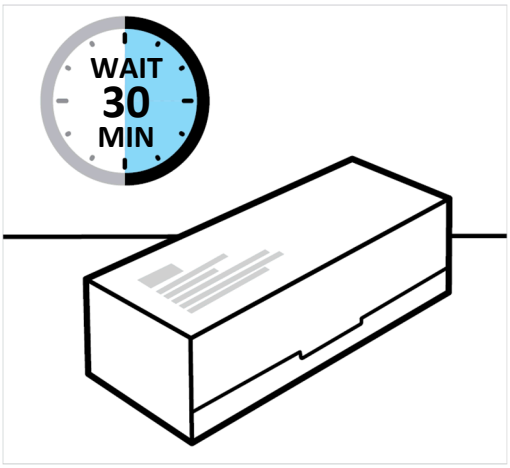
Not provided in the carton:

- **Alcohol swabs**
- **Cotton balls** or **gauze pads**
- **Adhesive bandages**
- **Sharps container** (See Step 4)

1. Get ready

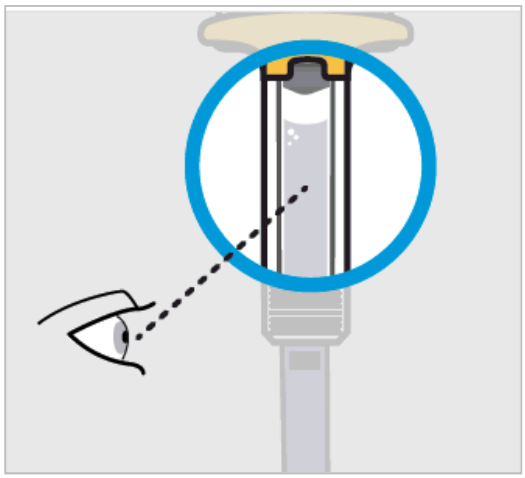


Check your dose to see if you will need to use 1 or 2 pre-filled syringes and inspect carton(s)
Remove the carton(s) with the pre-filled syringe from the refrigerator.
Check the expiration ('EXP') date.
Do not use the pre-filled syringe if the expiration date has passed or if the seal on the carton is broken.
Call your healthcare professional for a new pre-filled syringe.



Allow TREMFYA® to come to room temperature
Let the carton(s) sit on a flat surface at room temperature for approximately **30 minutes** before use.
Do not warm the pre-filled syringe(s) any other way.

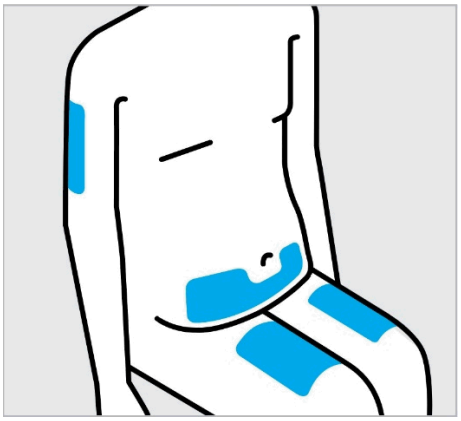
2. Prepare for your injection



Inspect liquid to see that it is clear to slightly yellow
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 air bubbles. This is normal.

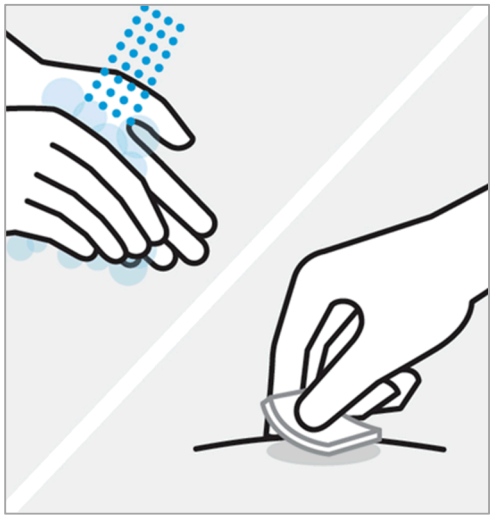
Do not inject if the liquid is:
- cloudy or
- discolored or
- has large particles

Do not use the pre-filled syringe if it is dropped.
If you are uncertain, call your healthcare professional for a new pre-filled syringe.



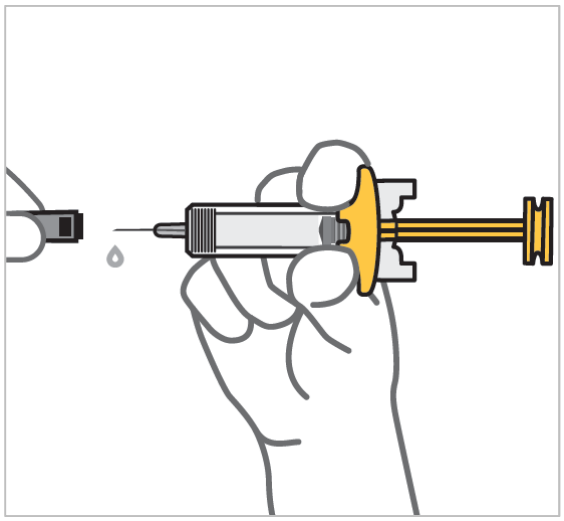
Choose injection site
Select a site from the following areas for your injection:
- Front of thighs
- Lower stomach area (lower abdomen)
  Do not use the 2-inch (5-centimetre) area around your belly-button
- Back of upper arms (if a caregiver is giving you the injection)

If you need to give 2 injections to complete your dose, choose different areas or leave at least 2 inches (5-centimetres) between injection sites.
Do not inject into skin that is tender, bruised, red, scaly, thick or hard.
Avoid areas with scars or stretch marks.

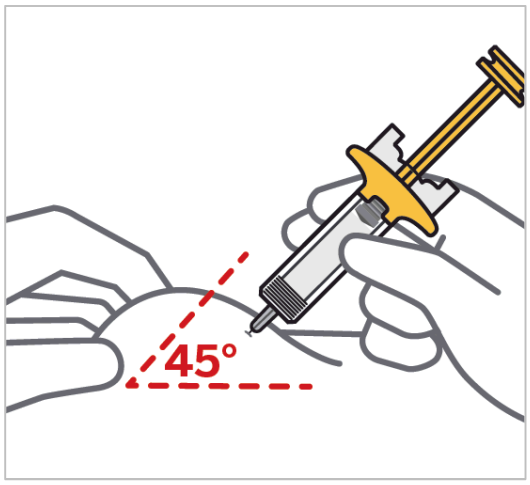


Wash hands and clean injection site
Wash your hands well with soap and warm water.
Wipe your chosen injection site with an alcohol swab and allow it to dry.
Do not touch, fan, or blow on the injection site after you have cleaned it.

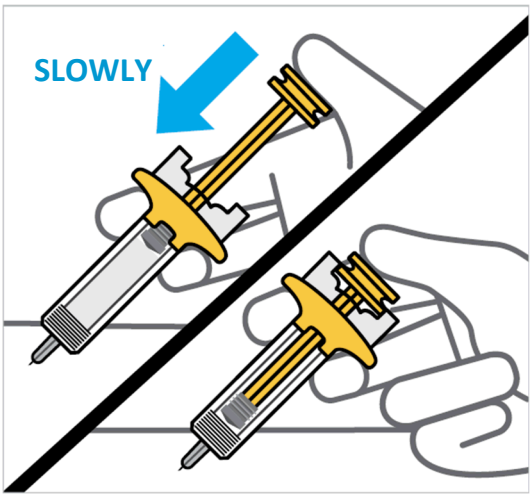
3. Inject TREMFYA® using the pre-filled syringe



Remove needle cover when you are ready to inject
Hold the pre-filled syringe by the body and pull needle cover straight off.
It is normal to see a few drops of liquid.
Inject TREMFYA® 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 pre-filled syringe if it is dropped. Call your healthcare professional for a new pre-filled syringe.
Do not hold or pull the plunger at any time.



Pinch injection site and insert needle at about a 45-degree angle
It is important to pinch enough skin to inject under the skin and not into muscle.
Insert needle with a quick dart-like motion.

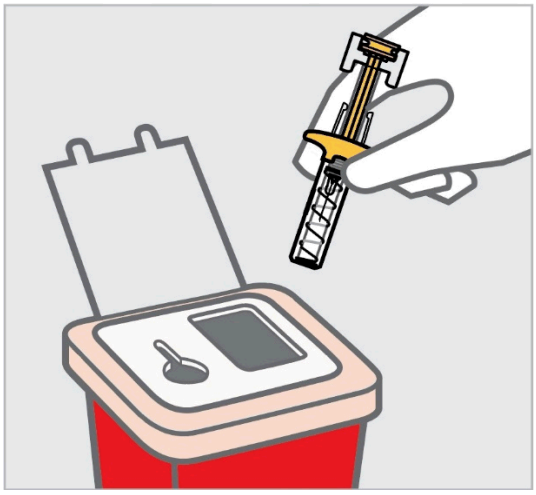


Slowly press plunger all the way down until it stops to inject all of the liquid
You will feel some resistance as you press the plunger, this is normal.

Release pressure from plunger to remove the needle from the skin
The needle will retract into the device and lock into place.
If your prescribed dose requires two injections, repeat Steps 2 to 4 with the second pre-filled syringe.

4. After your injection

Check injection site
There may be a small amount of blood or liquid at the injection site.
Gently hold pressure over the injection site with a cotton ball or gauze pad until any bleeding stops.
Do not rub the injection site. If needed, cover the injection site with a bandage.
Your injection is now complete!



Throw away the used pre-filled syringe
Put the used pre-filled syringe in a sharps disposal container right away after use.
Make sure you dispose of the bin as instructed by your healthcare professional when the container is full.
Do not throw away (dispose of) your pre-filled syringe in your household waste.
Do not recycle your used sharps disposal container.

Need Help?

Call your healthcare professional to talk about any questions you may have. For questions or concerns visit the manufacturer's website 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: July 2025

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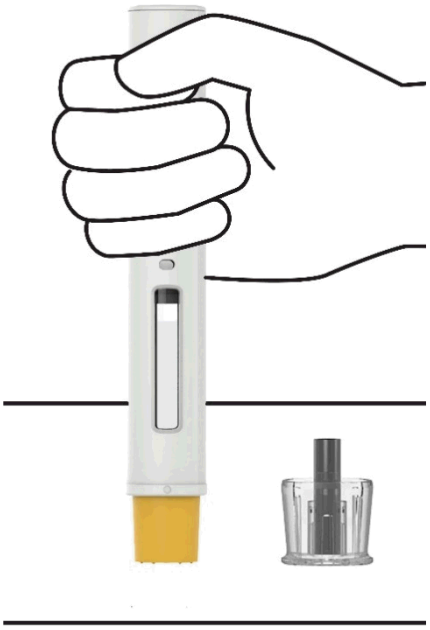
INSTRUCTIONS FOR USE (TREMFYA® 200 mg Pen)

PrTREMFYA®
(guselkumab injection)

200 mg Pre-filled Pen



SINGLE-USE DEVICE

PLEASE READ THESE INSTRUCTIONS BEFORE USE
Important

TREMFYA® comes in a single-use pre-filled pen containing one 200 mg dose.

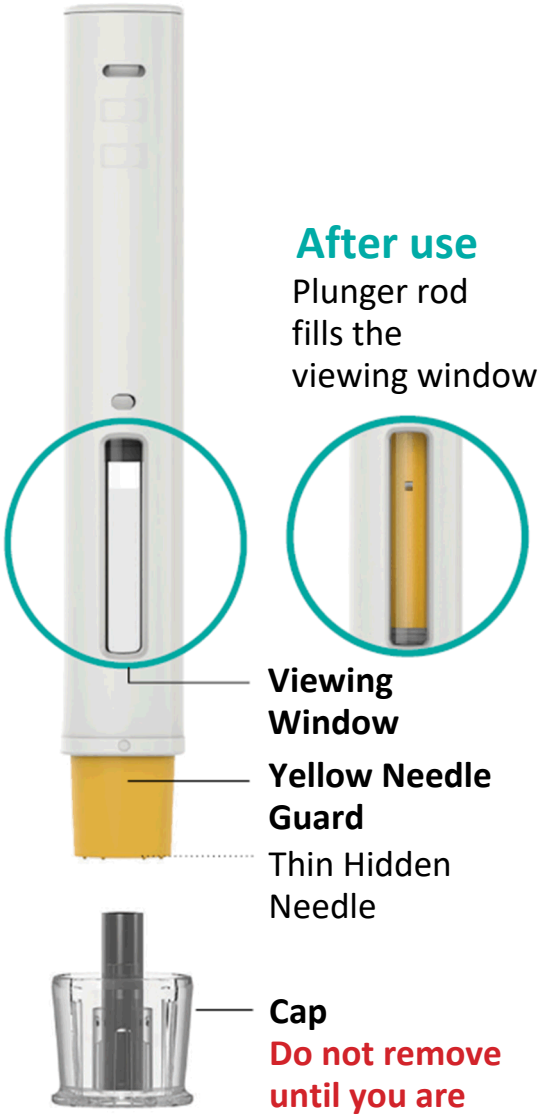
Your healthcare professional will tell you if you will need to use 1 or 2 pens.

If your healthcare professional 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 pen.
Please read these Instructions for Use before using the TREMFYA® pen and each time you get a new pen. There may be new information. This instruction guide does not take the place of talking with your healthcare professional 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 healthcare professional.
Each TREMFYA® pen can only be used one time. Throw the used pen away (see Step 4) after one dose, even if there is still medicine left in it. Do not reuse your pen.


Storage information
Store in refrigerator at 2° to 8°C.
Do not freeze.
Do not shake your pen.
Keep your TREMFYA® pen in the original carton to protect from light and physical damage.
Keep TREMFYA® and all medicines out of reach of children.

TREMFYA® pen at-a-glance

Before use



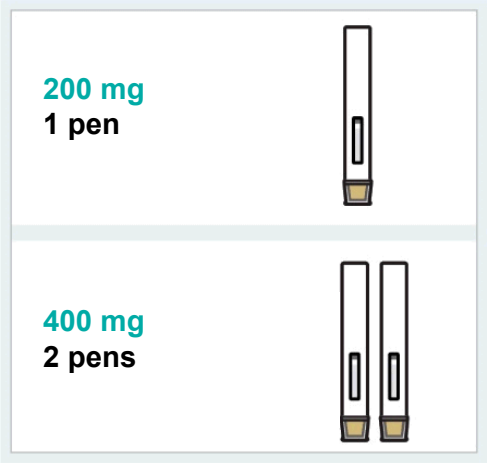
You will need:

- **1 or 2 Pens based on the dose prescribed by your healthcare professional**

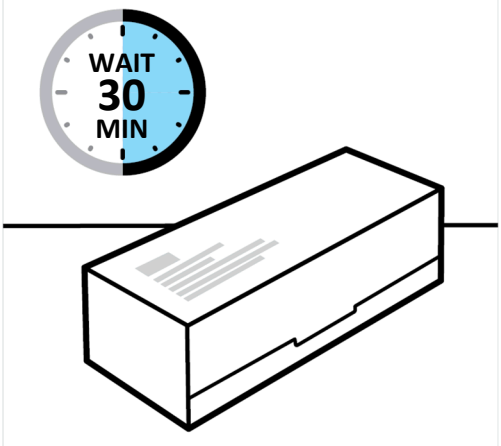
Not provided in the carton:

- **Alcohol swabs**
- **Cotton balls** or **gauze pads**
- **Adhesive bandages**
- **Sharps container** (See Step 4)

1. Get ready

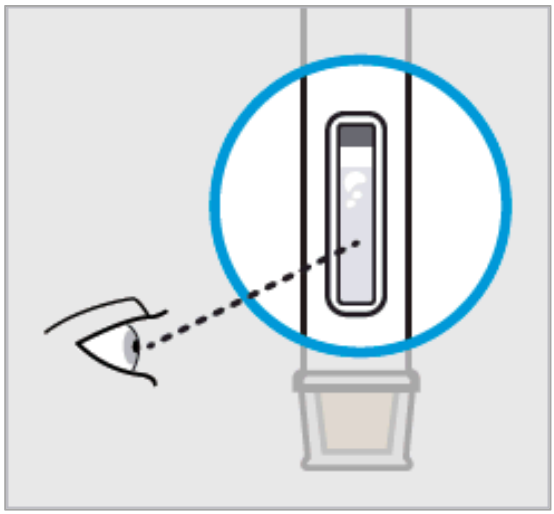


Check your dose to see if you will need to use 1 or 2 pens and inspect carton(s)
Remove the carton(s) with the pen from the refrigerator.
Check the expiration date ('EXP') on the carton.
Do not use the pen if the expiration date has passed or if the seal on the carton is broken.
Call your healthcare professional for a new pen.



Allow TREMFYA® to come to room temperature
Let the carton(s) sit on a flat surface at room temperature for approximately **30 minutes** before use.
Do not warm the pen(s) any other way.

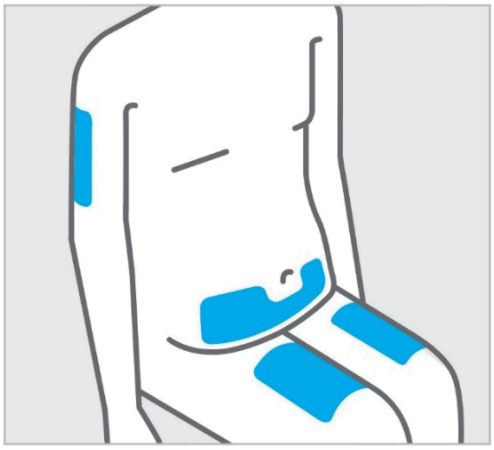
2. Prepare for your injection



Inspect liquid in window to see that it is clear to slightly yellow
Take the pen 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 air bubbles. This is normal.

Do not inject if the liquid is:
- cloudy or
- discolored or,
- has large particles

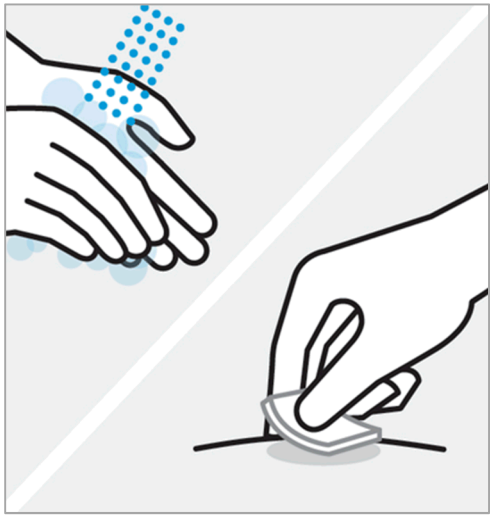
If you are uncertain, call your healthcare professional for a new pen.



Choose injection site
Select from the following areas for your injection:

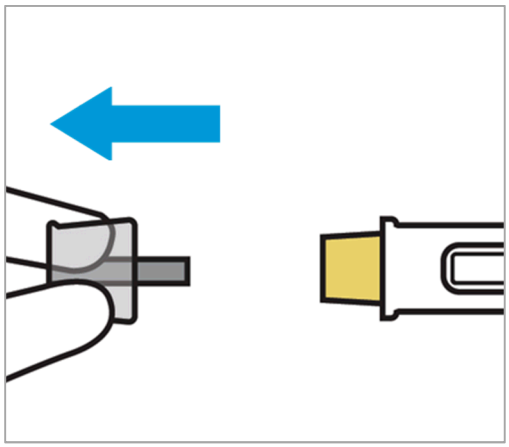
- Front of thighs
- Lower stomach area (lower abdomen)
  Do not use the 2-inch (5-centimetre) area around your belly-button.
- Back of upper arms (if a caregiver is giving you the injection)

If you need to give 2 injections to complete your dose, choose different areas or leave at least 2 inches (5-centimetres) between injection sites.
Do not inject into skin that is tender, bruised, red, scaly, thick or hard.
Avoid areas with scars or stretch marks.



Wash hands and 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.

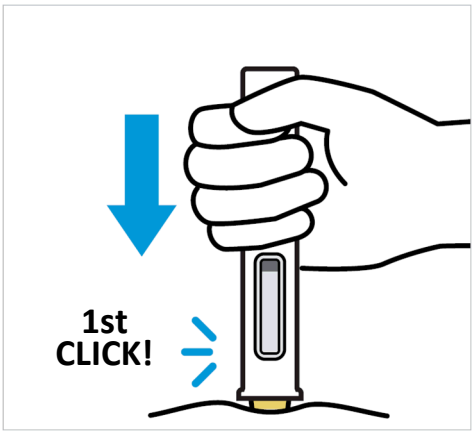
3. Inject TREMFYA® using the pen



Remove cap when you are ready to inject

Do Not Touch Yellow Needle Guard!
This may start the injection and you will not receive the dose.

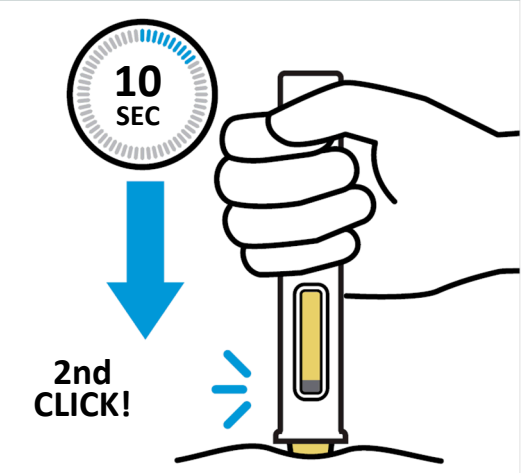
Pull the cap straight off. It is normal to see a few drops of liquid.
Inject TREMFYA® within 5 minutes of removing cap.
Do not put the cap back on as this may damage the needle.
Do not use the pen if it is dropped after removing the cap.
Call your healthcare professional for a new pen.



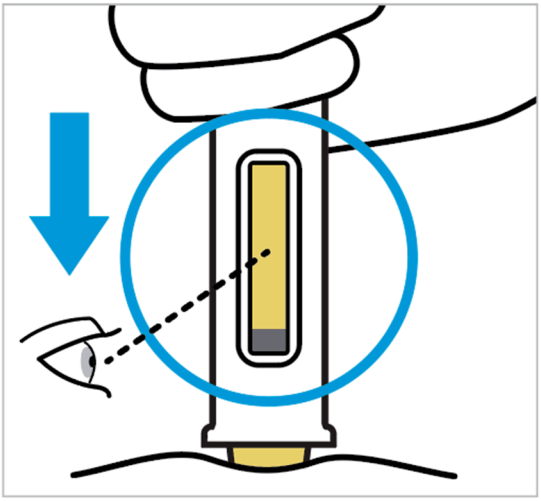
Position pen straight onto the injection site then push and hold pen

Do Not Lift The Pen During Injection!
If you do, the yellow needle guard will lock and the full dose will not be delivered.

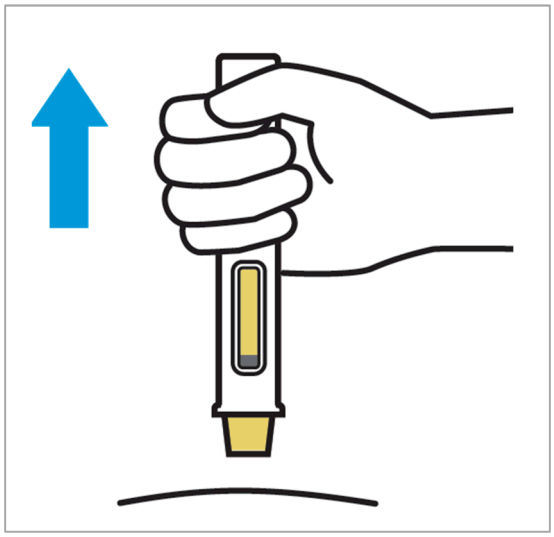
Position the pen straight onto the injection site with the yellow needle guard against the skin and the viewing window facing you.
Press down on the pen and keep holding it down against the skin.
You will hear the first click.



Keep holding the pen firmly against the skin for about 10 seconds to hear a second click
You are almost done.



Keep holding firmly against the skin and confirm the injection is complete
The injection is complete when the plunger rod stops moving and fills the viewing window.



Lift straight up

If your prescribed dose requires two injections, repeat Steps 2 to 4 with the second pen.

4. After your injection

Check injection site
There may be a small amount of blood or liquid at the injection site.
Gently hold pressure over the injection site with a cotton ball or gauze pad until any bleeding stops.
Do not rub the injection site. If needed, cover the injection site with a bandage.
Your injection is now complete!

Throw away the used pen and cap
Put your used pen and cap in a sharps disposal container right away after use.
Make sure you dispose of the bin as instructed by your healthcare professional when the container is full.
Do not throw away (dispose of) your pen in your household waste.
Do not recycle your used sharps disposal container.

Need Help?

Call your healthcare professional to talk about any questions you may have. For questions or concerns visit the manufacturer's website 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: July 2025

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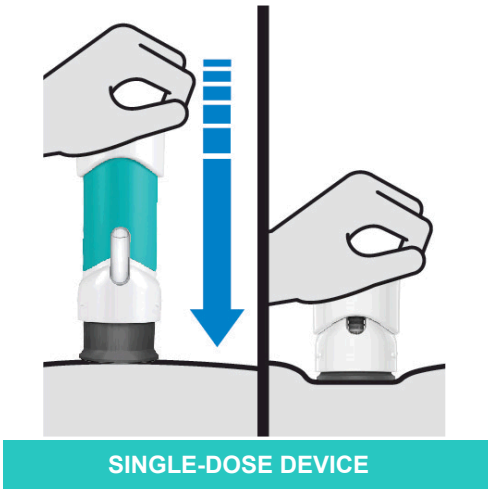
INSTRUCTIONS FOR USE (TREMFYA One-Press®)

PrTREMFYA 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 healthcare professional 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 healthcare professional 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 healthcare professional.

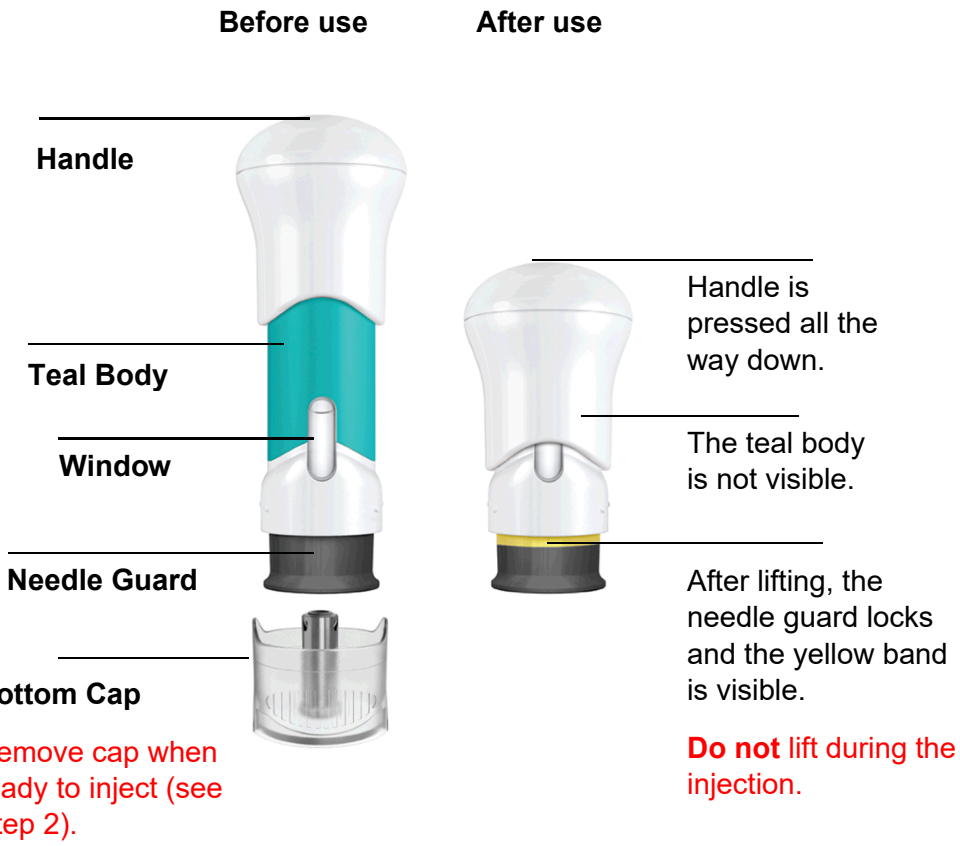
During injection, push handle all the way down until teal body is not visible to inject the full dose.

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

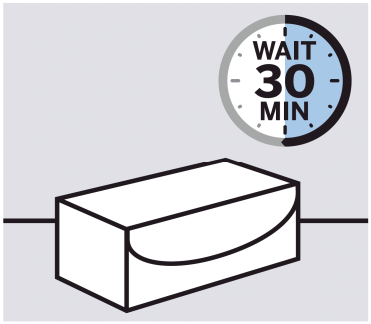
Store in refrigerator at 2˚ to 8˚C.
Do not freeze.
Do not shake at any time.
Keep TREMFYA One-Press® and all medicines out of reach and sight of children.
Keep TREMFYA One-Press® in the original carton to protect from light and physical damage.

TREMFYA One-Press® at-a-glance

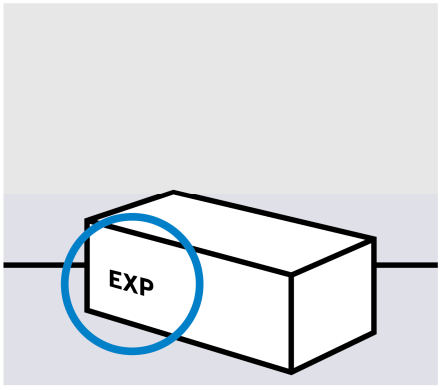


You will need these supplies:
- **1 Alcohol swab**
- **1 Cotton ball** or **gauze pad**
- **1 Adhesive bandage**
- **1 Sharps container** (See Step 3)

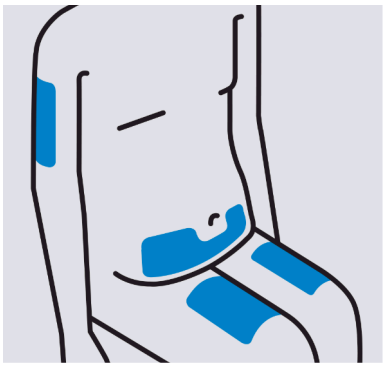
1. Prepare for your injection



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.



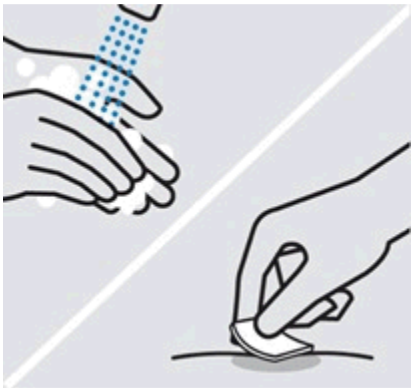
Check the expiration date ('EXP') on the carton.
Do not use if the expiration date has passed.
Do not inject if the seal on the carton is broken.
Call your healthcare professional for a new **TREMFYA One-Press®**.



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.

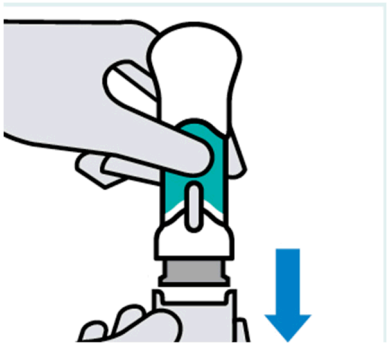
Clean injection site
Wipe your chosen injection site with an alcohol swab and allow it to dry.
Do not touch, fan or blow on the injection site after you have cleaned it.

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:

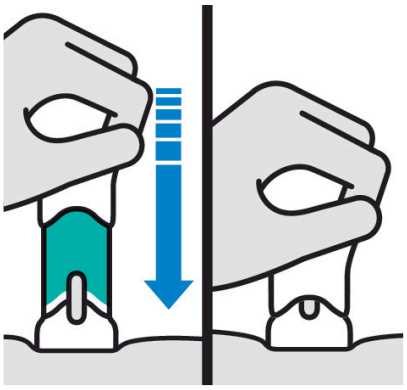
- cloudy, or
- discoloured, or
- has large particles.

If you are uncertain, call your healthcare professional 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 healthcare professional for a new **TREMFYA One-Press®**.



Place straight on skin

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

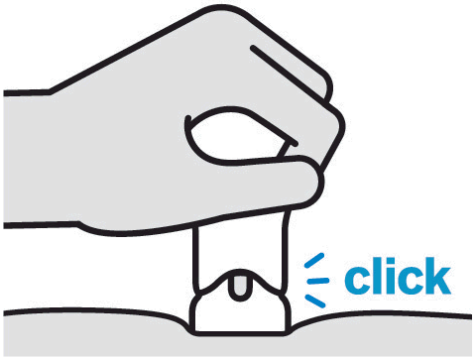
DO NOT LIFT THE ONE-PRESS INJECTOR DURING THE INJECTION!

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.

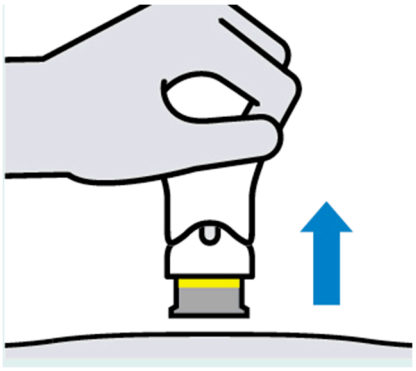
If you feel resistance, keep pushing. This is normal.

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



Confirm injection is complete
Injection is complete when:

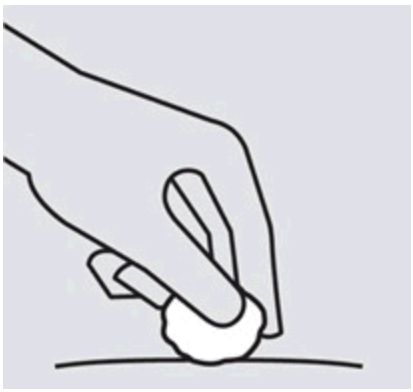
- **The teal body is no longer visible**
- You cannot press the handle down anymore
- You may hear a click



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 healthcare professional 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 healthcare professional to talk about any questions you may have. For questions or concerns visit the manufacturer's website www.janssen.com/canada, or call 1-800-567-3331 or 1-800-387-8781.

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PATIENT MEDICATION INFORMATION (TREMFYA® I.V.)

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrTREMFYA® I.V.

(guselkumab for injection)
Solution for intravenous injection

200 mg/ 20 mL

Read this carefully before you start taking **TREMFYA® I.V.** 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® I.V.**

What is TREMFYA® I.V. used for?

- **Crohn's Disease**

TREMFYA® I.V. is used to treat adults with moderately to severely active Crohn's disease, an inflammatory disease of the bowel. Using TREMFYA® I.V. in Crohn's disease can benefit you by reducing the signs and symptoms of the disease such as diarrhea, abdominal pain, and the inflammation of your intestinal lining. This may enable your normal daily activities and reduce fatigue.

- **Ulcerative Colitis**

TREMFYA® I.V. is used to treat adults with moderately to severely active ulcerative colitis, an inflammatory disease of the bowel. Using TREMFYA® I.V. in ulcerative colitis will benefit you by reducing the signs and symptoms of the disease including bloody stools, the need to rush to and the number of times you go to the toilet, abdominal pain and the inflammation of your intestinal lining. This may enable your normal daily activities and reduce fatigue.

How does TREMFYA® I.V. work?

TREMFYA® I.V. 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 Crohn's disease and ulcerative colitis.

What are the ingredients in TREMFYA® I.V.?

Medicinal ingredients: guselkumab

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

TREMFYA® I.V. comes in the following dosage forms:

TREMFYA® I.V. is supplied as a 200 mg/20 mL (10mg/mL) solution in a single-dose vial.

Do not use TREMFYA® I.V. if:

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

If you think you are allergic, ask your healthcare professional for advice before using TREMFYA® I.V.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take TREMFYA® I.V. 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® I.V. 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
    - diarrhea or stomach pain
- have recently had a vaccination or if you are due to have a vaccination during treatment with TREMFYA® I.V. You should not be given certain types of vaccines (live vaccines) while using TREMFYA®/TREMFYA® I.V.
- 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® I.V. and for at least 12 weeks after the last TREMFYA®/TREMFYA® I.V. dose. Talk to your healthcare professional about your contraception options.
- are breast-feeding or plan to breast-feed. You and your healthcare professional should decide if you will breast-feed while using TREMFYA®/TREMFYA® I.V.

Look out for infections and allergic reactions

- Do not use TREMFYA® I.V. if you have any symptoms of infection unless you are instructed by your healthcare provider.
- **After starting TREMFYA® I.V., 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® I.V. Tell your healthcare professional or seek medical help immediately if you experience these symptoms**.

Children and adolescents (below the age of 18 years)
TREMFYA® I.V. 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® I.V.:

TREMFYA® I.V. will be given by your healthcare professional.

Usual dose:

Crohn's Disease

Treatment start

Treatment start can be given by either intravenous infusion (drip in a vein in your arm) or administered subcutaneously (injections under the skin).

Intravenous Infusion (TREMFYA® I.V.):

- The first dose is 200 mg and will be given by your healthcare provider by intravenous infusion over at least 1 hour.
- After the first dose, you will have the second dose by intravenous infusion 4 weeks later, and then a third dose by intravenous infusion after an additional 4 weeks.

Subcutaneous administration (TREMFYA®):

- The first dose is 400 mg and will be given by injections under the skin at different locations of the body (refer to the Patient Medication Information for TREMFYA®).
- After the first dose, you will have a second 400 mg dose 4 weeks later and then a third 400 mg dose after an additional 4 weeks.

Maintenance therapy (TREMFYA®)

A maintenance dose will be given by injection under the skin (subcutaneous injection) either with 100 mg or 200 mg (refer to the Patient Medication Information for TREMFYA®). Your healthcare provider will decide which maintenance dose you will receive:

- A dose of 100 mg will be given 8 weeks after the third treatment start dose, followed by a dose every 8 weeks.
- A dose of 200 mg will be given 4 weeks after the third treatment start dose, followed by a dose every 4 weeks.

Ulcerative Colitis

Treatment start (TREMFYA® I.V.)

- The first dose is 200 mg and will be given by your healthcare provider by intravenous infusion (drip in a vein in your arm) over at least 1 hour.
- After the first dose, you will have the second dose by intravenous infusion 4 weeks later, and then a third dose by intravenous infusion after an additional 4 weeks.

Maintenance therapy (TREMFYA®)

A maintenance dose will be given by injection under the skin (subcutaneous injection) either with 100 mg or 200 mg (refer to the Patient Medication Information for TREMFYA®). Your healthcare provider will decide which maintenance dose you will receive:

- A dose of 100 mg will be given 8 weeks after the third treatment start dose, followed by a dose every 8 weeks.
- A dose of 200 mg will be given 4 weeks after the third treatment start dose, followed by a dose every 4 weeks.

Your healthcare professional will regularly monitor your condition to check that the treatment is having the desired effect.

You should not stop using TREMFYA® I.V. unless you think it is causing a severe side effect. Speak to your healthcare professional as soon as possible if this happens.

Overdose:

In the event of overdosage, monitor the patient for any signs or symptoms of adverse reactions and administer appropriate symptomatic treatment immediately.

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

Missed dose:

If you forget or miss an appointment to receive TREMFYA® I.V., contact your healthcare professional.

What are possible side effects from using TREMFYA® I.V.?

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® I.V. 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® I.V. in the refrigerator between 2°C to 8°C (36°F to 46°F).

Do not freeze. Do not use if TREMFYA® I.V. has been frozen.

Do not shake TREMFYA® I.V.

Store in original packaging to protect from light until use.

Keep out of reach and sight of children.

Do not use TREMFYA® I.V.:

- 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® I.V. is for single use only.

If you want more information about TREMFYA® I.V.:

- Talk to your healthcare professional
- For questions or concerns, contact the manufacturer, Janssen Inc. (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://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website www.janssen.com/canada, or by contacting the manufacturer at: 1-800-567-3331 or 1-800-387-8781.

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