

**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

## **1. NAME OF THE MEDICINAL PRODUCT**

Tremfya 100 mg solution for injection in pre-filled syringe.  
Tremfya 100 mg solution for injection in pre-filled pen.

## **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Tremfya 100 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 100 mg of guselkumab in 1 mL solution.

Tremfya 100 mg solution for injection in pre-filled pen

Each pre-filled pen contains 100 mg of guselkumab in 1 mL solution.

Guselkumab is a fully human immunoglobulin G1 lamda (IgG1 $\lambda$ ) monoclonal antibody (mAb) to the interleukin (IL)-23 protein, produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology.

For the full list of excipients, see section 6.1.

## **3. PHARMACEUTICAL FORM**

Solution for injection (injection)

The solution is clear and colourless to light yellow.

## **4. CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

Plaque psoriasis

Tremfya is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

Psoriatic arthritis

Tremfya, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adult patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy (see section 5.1).

### **4.2 Posology and method of administration**

Tremfya is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of conditions for which Tremfya is indicated.

## Posology

### *Plaque psoriasis*

The recommended dose of Tremfya is 100 mg by subcutaneous injection at weeks 0 and 4, followed by a maintenance dose every 8 weeks.

Consideration should be given to discontinuing treatment in patients who have shown no response after 16 weeks of treatment.

### *Psoriatic arthritis*

The recommended dose of Tremfya is 100 mg by subcutaneous injection at weeks 0 and 4, followed by a maintenance dose every 8 weeks. For patients at high risk for joint damage according to clinical judgement, a dose of 100 mg every 4 weeks may be considered (see section 5.1).

Consideration should be given to discontinuing treatment in patients who have shown no response after 24 weeks of treatment.

## Special Populations

### *Elderly ( $\geq 65$ years)*

No dose adjustment is required (see section 5.2).

There is limited information in subjects aged  $\geq 65$  years and very limited information in subjects aged  $\geq 75$  years (see section 5.2).

### *Renal or hepatic impairment*

Tremfya has not been studied in these patient populations. No dose recommendations can be made. For further information on elimination of guselkumab, see section 5.2.

### *Paediatric population*

The safety and efficacy of Tremfya in children and adolescents below the age of 18 years have not been established. No data are available.

### Method of administration

Subcutaneous use. If possible, areas of the skin that show psoriasis should be avoided as injection sites.

After proper training in subcutaneous injection technique, patients may inject Tremfya if a physician determines that this is appropriate. However, the physician should ensure appropriate medical follow-up of patients. Patients should be instructed to inject the full amount of Tremfya according to the 'Instructions for use' provided in the carton.

For further instructions on preparation and special precautions for handling, see section 6.6 and the 'Instructions for use' leaflet.

## **4.3 Contraindications**

Serious hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Clinically important active infections (e.g., active tuberculosis, see section 4.4).

## **4.4 Special warnings and precautions for use**

### Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

### Infections

Tremfya may increase the risk of infection. Treatment with Tremfya should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated.

Patients treated with Tremfya should be instructed 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, the patient should be monitored closely and Tremfya should be discontinued until the infection resolves.

#### Pre-treatment evaluation for tuberculosis

Prior to initiating treatment with Tremfya, patients should be evaluated for tuberculosis (TB) infection. Patients receiving Tremfya should be monitored for signs and symptoms of active TB during and after treatment. Anti-TB therapy should be considered prior to initiating Tremfya in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed.

#### Hypersensitivity

Serious hypersensitivity reactions, including anaphylaxis, have been reported in the post-marketing setting. Some serious hypersensitivity reactions occurred several days after treatment with guselkumab, including cases with urticaria and dyspnoea. If a serious hypersensitivity reaction occurs, administration of Tremfya should be discontinued immediately and appropriate therapy initiated.

#### Hepatic Transaminase Elevations

In psoriatic arthritis clinical studies, an increased incidence of liver enzyme elevations was observed in patients treated with Tremfya q4w compared to patients treated with Tremfya q8w or placebo (see section 4.8, Table 2).

When prescribing Tremfya q4w in psoriatic arthritis, it is recommended to evaluate liver enzymes at baseline and thereafter according to routine patient management. If increases in ALT or AST are observed and drug-induced liver injury is suspected, Tremfya should be temporarily interrupted until this diagnosis is excluded.

#### Immunisations

Prior to initiating therapy with Tremfya, completion of all appropriate immunisations should be considered according to current immunisation guidelines. Live vaccines should not be used concurrently in patients treated with Tremfya. No data are available on the response to live or inactive vaccines.

Before live viral or live bacterial vaccination, treatment with Tremfya should be withheld for at least 12 weeks after the last dose and can be resumed at least 2 weeks after vaccination. Prescribers should consult the Summary of Product Characteristics of the specific vaccine for additional information and guidance on concomitant use of immunosuppressive agents post-vaccination.

### **4.5 Interaction with other medicinal products and other forms of interaction**

#### Interactions with CYP450 substrates

In a Phase 1 study in subjects with moderate to severe plaque psoriasis, changes in systemic exposures ( $C_{max}$  and  $AUC_{inf}$ ) of midazolam, S-warfarin, omeprazole, dextromethorphan, and caffeine after a single dose of guselkumab were not clinically relevant, indicating that drug interactions between guselkumab and substrates of various CYP enzymes (CYP3A4, CYP2C9, CYP2C19, CYP2D6, and CYP1A2) are unlikely. There is no need for dose adjustment when co-administering guselkumab and CYP450 substrates.

#### Concomitant immunosuppressive therapy or phototherapy

In psoriasis studies, the safety and efficacy of Tremfya in combination with immunosuppressants, including biologics, or phototherapy have not been evaluated.

## 4.6 Fertility, pregnancy and lactation

### Women of childbearing potential

Women of childbearing potential should use effective methods of contraception during treatment and for at least 12 weeks after treatment.

### Pregnancy

There are no data from the use of guselkumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Tremfya in pregnancy.

### Breast-feeding

It is unknown whether guselkumab is excreted in human milk. Human IgGs are known to be excreted in breast milk during the first few days after birth, and decrease to low concentrations soon afterwards; consequently, a risk to the breast-fed infant during this period cannot be excluded. A decision should be made whether to discontinue, or abstain from initiating treatment with Tremfya, taking into account the benefit of breast-feeding to the child and the benefit of Tremfya therapy to the woman. See section 5.3 for information on the excretion of guselkumab in animal (cynomolgus monkey) milk.

### Fertility

The effect of guselkumab on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility (see section 5.3).

## 4.7 Effects on ability to drive and use machines

Tremfya has no or negligible influence on the ability to drive and use machines.

## 4.8 Undesirable effects

### Summary of the safety profile

The most common adverse drug reaction (ADR) was upper respiratory infection.

### Tabulated list of adverse reactions

Table 1 provides a list of adverse reactions from psoriasis and psoriatic arthritis clinical studies as well as from post-marketing experience. The adverse reactions are classified by MedDRA System Organ Class and frequency, using the following convention: very common ( $\geq 1/10$ ), common ( $\geq 1/100$  to  $< 1/10$ ), uncommon ( $\geq 1/1,000$  to  $< 1/100$ ), rare ( $\geq 1/10,000$  to  $< 1/1,000$ ), very rare ( $< 1/10,000$ ), not known (cannot be estimated from the available data).

**Table 1: List of adverse reactions**

System Organ Class	Frequency	ADR
Infections and infestations	Very common	Respiratory tract infections
	Uncommon	Herpes simplex infections
	Uncommon	Tinea infections
Investigations	Uncommon	Gastroenteritis
	Common	Transaminases increased
	Uncommon	Neutrophil count decreased
Immune system disorders	Uncommon	Hypersensitivity
	Uncommon	Anaphylaxis
Nervous system disorders	Common	Headache
Gastrointestinal disorders	Common	Diarrhoea
Skin and subcutaneous tissue disorders	Uncommon	Urticaria
	Uncommon	Rash

Musculoskeletal and connective tissue disorders	Common	Arthralgia
General disorders and administration site conditions	Common	Injection site reactions

#### Description of selected adverse reactions

##### *Transaminases Increased*

In two phase III psoriatic arthritis clinical studies, through the placebo-controlled period, increased transaminases (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) were reported more frequently as adverse events in the Tremfya-treated groups (8.6% in the q4w group and 8.3% in the q8w group) than in the placebo group (4.6%).

Based on laboratory assessments, most transaminase increases were  $\leq 3$  x upper limit of normal (ULN). Transaminase increases from  $> 3$  to  $\leq 5$  x ULN and  $> 5$  x ULN were low in frequency, occurring more often in the Tremfya q4w group compared with the Tremfya q8w group (Table 2). Through 1 year, in most cases, the increase in transaminases was transient and did not lead to discontinuation of treatment.

**Table 2: Frequency of patients with transaminase increases post-baseline in two Phase III psoriatic arthritis clinical studies**

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

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

<sup>b</sup> patients randomized to Tremfya at baseline

##### *Neutrophil count decreased*

In two phase III psoriatic arthritis clinical studies, through the placebo-controlled period, decreased neutrophil count was reported more frequently as an adverse event in the Tremfya-treated group (0.9%) than in the placebo group (0%). In most cases, the decrease in blood neutrophil count was mild, transient, not associated with infection and did not lead to discontinuation of treatment.

##### *Gastroenteritis*

In two phase III psoriasis clinical studies through the placebo-controlled period, gastroenteritis occurred more frequently in the Tremfya-treated group (1.1%) than in the placebo group (0.7%). Through Week 156, 4.9% of all Tremfya-treated patients reported gastroenteritis. Adverse reactions of gastroenteritis were non-serious and did not lead to discontinuation of Tremfya through Week 156. Gastroenteritis rates observed in psoriatic arthritis clinical studies through the placebo-controlled period were similar to those observed in the psoriasis clinical studies.

##### *Injection site reactions*

In two phase III psoriasis clinical studies through Week 48, 0.7% of Tremfya injections and 0.3% of placebo injections were associated with injection site reactions. Through Week 156, 0.5% of Tremfya injections were associated with injection site reactions. Adverse reactions of injection site erythema and injection site pain were the most commonly reported events of injection site reaction and were generally mild to moderate in severity; none were serious, and none led to discontinuation of Tremfya.

In two phase III psoriatic arthritis clinical studies through Week 24, the number of subjects that reported 1 or more injection site reactions was low and slightly higher in the Tremfya groups than in the placebo group; 5 (1.3%) subjects in the Tremfya q8w group, 4 (1.1%) subjects in the Tremfya q4w group, and 1 (0.3%) subject in the placebo group. One subject discontinued Tremfya due to an injection site reaction during the placebo-controlled period of the psoriatic arthritis clinical studies. Overall, the rate of injections associated with injection site reactions observed in psoriatic arthritis clinical studies through the placebo-controlled period similar to rates observed in the psoriasis clinical studies.

#### *Immunogenicity*

The immunogenicity of Tremfya was evaluated using a sensitive and drug-tolerant immunoassay.

#### *Plaque psoriasis*

In pooled phase II and phase III analyses in patients with psoriasis, fewer than 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. In pooled phase III analyses, approximately 9% of patients treated with Tremfya developed antidrug antibodies in up to 156 weeks of treatment. Antidrug antibodies were not associated with lower efficacy or development of injection-site reactions.

#### Psoriatic arthritis

In pooled phase III analyses in patients with psoriatic arthritis, 2% (n=15) of patients treated with Tremfya developed antidrug antibodies in up to 24 weeks of treatment. Of these patients, 1 patient had antibodies that were classified as neutralizing. None of these patients developed injection site reactions. Overall, the small number of patients with antidrug antibodies limits definitive conclusion of the effect of immunogenicity on the pharmacokinetics, efficacy or safety of guselkumab in patients with psoriatic arthritis.

#### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in [Appendix V](#).

## **4.9 Overdose**

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

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC16.

#### Mechanism of action

Guselkumab is a human IgG1 $\lambda$  monoclonal antibody (mAb) that binds selectively to the interleukin 23 (IL-23) protein with high specificity and affinity. IL-23, a regulatory cytokine, affects the differentiation, expansion, and survival of T cell subsets, (e.g., Th17 cells and Tc17 cells) and innate immune cell subsets, which represent sources of effector cytokines, including IL-17A, IL-17F and IL-22 that drive inflammatory disease. In humans, selective blockade of IL-23 was shown to normalize production of these cytokines.

Levels of IL-23 are elevated in the skin of patients with plaque psoriasis. In *in vitro* models, guselkumab was shown to inhibit the bioactivity of IL-23 by blocking its interaction with cell surface IL-23 receptor, disrupting IL-23-mediated signaling, activation and cytokine cascades. Guselkumab exerts clinical effects in plaque psoriasis and psoriatic arthritis through blockade of the IL-23 cytokine pathway.

#### Pharmacodynamic effects

In a phase I study, treatment with guselkumab resulted in reduced expression of IL-23/Th17 pathway genes and psoriasis-associated gene expression profiles, as shown by analyses of mRNA obtained from lesional skin biopsies of patients with plaque psoriasis at Week 12 compared to baseline. In the same phase I study, treatment with guselkumab resulted in improvement of histological measures of psoriasis at Week 12, including reductions in epidermal thickness and T-cell density. In addition, reduced serum IL-17A, IL-17F and IL-22 levels compared to placebo were observed in guselkumab treated patients in phase II and phase III plaque psoriasis studies. These results are consistent with the clinical benefit observed with guselkumab treatment in plaque psoriasis.

In psoriatic arthritis patients in phase III studies, serum levels of acute phase proteins C-reactive protein, serum amyloid A, and IL-6, and Th17 effector cytokines IL-17A, IL-17F and IL-22 were elevated at baseline. Guselkumab decreased the levels of these proteins within 4 weeks of initiation of treatment. Guselkumab further reduced the levels of these proteins by Week 24 compared to baseline and also to placebo.

#### Clinical efficacy and safety

##### Plaque psoriasis

The efficacy and safety of guselkumab was assessed in three randomised, double-blind, active controlled phase III studies in adult patients with moderate to severe plaque psoriasis, who were candidates for phototherapy or systemic therapy.

##### *VOYAGE 1 and VOYAGE 2*

Two studies (VOYAGE 1 and VOYAGE 2) evaluated the efficacy and safety of guselkumab versus placebo and adalimumab in 1829 adult patients. Patients randomised to guselkumab (N=825) received 100 mg at Weeks 0 and 4, and every 8 weeks (q8w) thereafter through Week 48 (VOYAGE 1) and Week 20 (VOYAGE 2). Patients randomised to adalimumab (N=582) received 80 mg at Week 0 and 40 mg at Week 1, followed by 40 mg every other week (q2w) through Week 48 (VOYAGE 1) and Week 23 (VOYAGE 2). In both studies, patients randomised to placebo (N=422) received guselkumab 100 mg at Weeks 16, 20 and q8w thereafter. In VOYAGE 1, all patients, including those randomised to adalimumab at Week 0, started to receive open-label guselkumab q8w at Week 52. In VOYAGE 2, patients randomised to guselkumab at Week 0 who were Psoriasis Area and Severity Index (PASI) 90 responders at Week 28 were re-randomised to either continue treatment with guselkumab q8w (maintenance treatment) or receive placebo (withdrawal treatment). Withdrawal patients re-initiated guselkumab (dosed at time of retreatment, 4 weeks later and q8w thereafter) when they experienced at least a 50% loss of their Week 28 PASI improvement. Patients randomised to adalimumab at Week 0 who were PASI 90 non-responders received guselkumab at Weeks 28, 32 and q8w thereafter. In VOYAGE 2, all patients started to receive open-label guselkumab q8w at Week 76.

Baseline disease characteristics were consistent for the study populations in VOYAGE 1 and 2 with a median body surface area (BSA) of 22% and 24%, a median baseline PASI score of 19 for both studies, a median baseline dermatology quality of life index (DLQI) score of 14 and 14.5, a baseline investigator global assessment (IGA) score of severe for 25% and 23% of patients, and a history of psoriatic arthritis for 19% and 18% of patients, respectively.

Of all patients included in VOYAGE 1 and 2, 32% and 29% were naïve to both conventional systemic and biologic 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



therapy, including 11% who had received at least one anti-tumour necrosis factor alpha (TNF $\alpha$ ) agent, and approximately 10% who had received an anti-IL-12/IL-23 agent.

The efficacy of guselkumab was evaluated with respect to overall skin disease, regional disease (scalp, hand and foot and nails) and quality of life and patient reported outcomes. The co-primary endpoints in VOYAGE 1 and 2 were the proportion of patients who achieved an IGA score of cleared or minimal (IGA 0/1) and a PASI 90 response at Week 16 versus placebo (see Table 3).

#### Overall skin disease

Treatment with guselkumab resulted in significant improvements in the measures of disease activity compared to placebo and adalimumab at Week 16 and compared to adalimumab at Weeks 24 and 48. The key efficacy results for the primary and major secondary study endpoints are shown in Table 3 below.

**Table 3: Summary of Clinical Responses in VOYAGE 1 and VOYAGE 2**

	Number of patients (%)					
	Placebo (N=174)	VOYAGE 1 Guselkumab (N=329)	Adalimumab (N=334)	Placebo (N=248)	VOYAGE 2 Guselkumab (N=496)	Adalimumab (N=248)
<b>Week 16</b>						
PASI 75	10 (5.7)	300 (91.2) <sup>a</sup>	244 (73.1) <sup>b</sup>	20 (8.1)	428 (86.3) <sup>a</sup>	170 (68.5) <sup>b</sup>
PASI 90	5 (2.9)	241 (73.3) <sup>c</sup>	166 (49.7) <sup>b</sup>	6 (2.4)	347 (70.0) <sup>c</sup>	116 (46.8) <sup>b</sup>
PASI 100	1 (0.6)	123 (37.4) <sup>a</sup>	57 (17.1) <sup>d</sup>	2 (0.8)	169 (34.1) <sup>a</sup>	51 (20.6) <sup>d</sup>
IGA 0/1	12 (6.9)	280 (85.1) <sup>c</sup>	220 (65.9) <sup>b</sup>	21 (8.5)	417 (84.1) <sup>c</sup>	168 (67.7) <sup>b</sup>
IGA 0	2 (1.1)	157 (47.7) <sup>a</sup>	88 (26.3) <sup>d</sup>	2 (0.8)	215 (43.3) <sup>a</sup>	71 (28.6) <sup>d</sup>
<b>Week 24</b>						
PASI 75	-	300 (91.2)	241 (72.2) <sup>e</sup>	-	442 (89.1)	176 (71.0) <sup>e</sup>
PASI 90	-	264 (80.2)	177 (53.0) <sup>b</sup>	-	373 (75.2)	136 (54.8) <sup>b</sup>
PASI 100	-	146 (44.4)	83 (24.9) <sup>e</sup>	-	219 (44.2)	66 (26.6) <sup>e</sup>
IGA 0/1	-	277 (84.2)	206 (61.7) <sup>b</sup>	-	414 (83.5)	161 (64.9) <sup>b</sup>
IGA 0	-	173 (52.6)	98 (29.3) <sup>b</sup>	-	257 (51.8)	78 (31.5) <sup>b</sup>
<b>Week 48</b>						
PASI 75	-	289 (87.8)	209 (62.6) <sup>e</sup>	-	-	-
PASI 90	-	251 (76.3)	160 (47.9) <sup>b</sup>	-	-	-
PASI 100	-	156 (47.4)	78 (23.4) <sup>e</sup>	-	-	-
IGA 0/1	-	265 (80.5)	185 (55.4) <sup>b</sup>	-	-	-
IGA 0	-	166 (50.5)	86 (25.7) <sup>b</sup>	-	-	-

<sup>a</sup> p < 0.001 for comparison between guselkumab and placebo.

<sup>b</sup> p < 0.001 for comparison between guselkumab and adalimumab for major secondary endpoints.

<sup>c</sup> p < 0.001 for the comparisons between guselkumab and placebo for the co-primary endpoints.

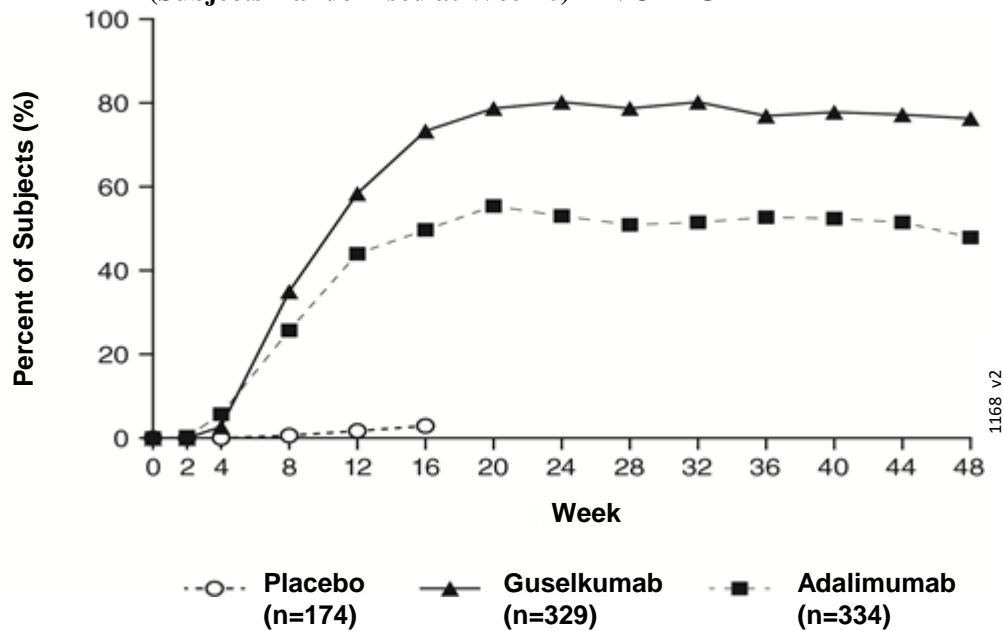
<sup>d</sup> comparisons between guselkumab and adalimumab were not performed.

<sup>e</sup> p < 0.001 for comparison between guselkumab and adalimumab.

#### Response over time

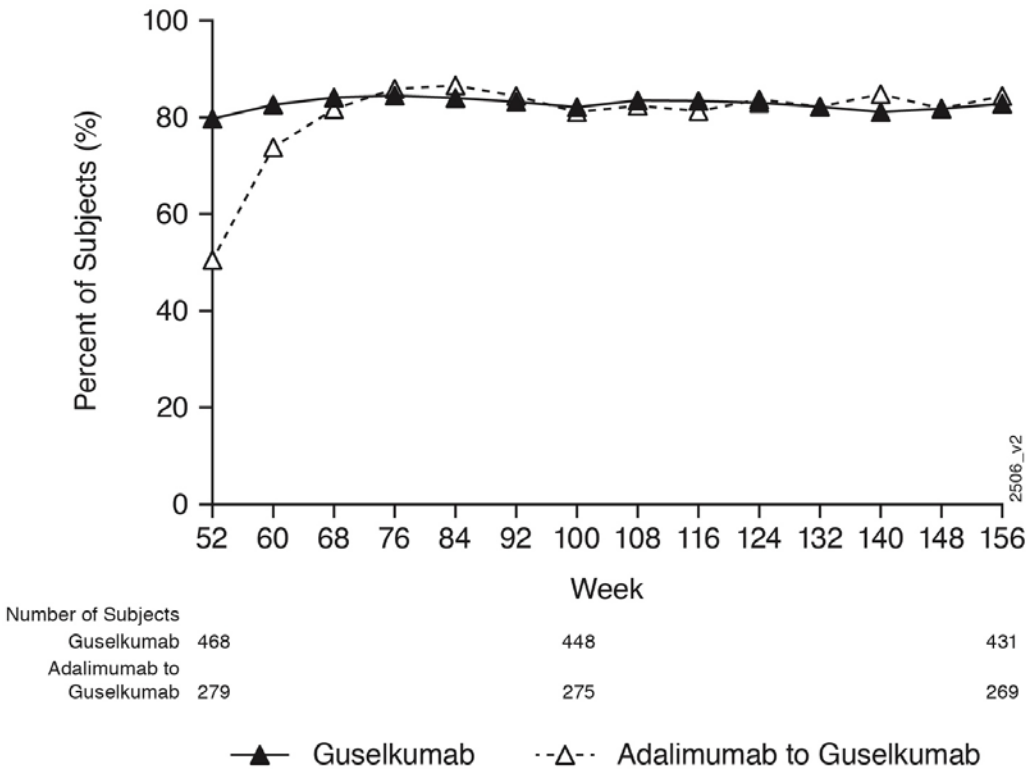
Guselkumab demonstrated rapid onset of efficacy, with a significantly higher percent improvement in PASI as compared with placebo as early as Week 2 (p < 0.001). The percentage of patients achieving a PASI 90 response was numerically higher for guselkumab than adalimumab starting at Week 8 with the difference reaching a maximum around Week 20 (VOYAGE 1 and 2) and maintained through Week 48 (VOYAGE 1) (see Figure 1).

**Figure 1: Percent of Subjects Who Achieved a PASI 90 Response Through Week 48 by Visit (Subjects Randomised at Week 0) in VOYAGE 1**



In VOYAGE 1, for patients receiving continuous guselkumab treatment, the PASI 90 response rate was maintained from Week 52 through Week 156. For patients randomised to adalimumab at Week 0 who crossed over to guselkumab at Week 52, the PASI 90 response rate increased from Week 52 through Week 76 and was then maintained through Week 156 (see Figure 2).

**Figure 2: Percent of Subjects Who Achieved a PASI 90 Response by Visit in the Open-Label Phase in VOYAGE 1**



The efficacy and safety of guselkumab was demonstrated regardless of age, gender, race, body weight, plaques location, PASI baseline severity, concurrent psoriatic arthritis, and previous treatment with a biologic therapy. Guselkumab was efficacious in conventional systemic-naïve, biologic-naïve, and biologic-exposed patients.

In VOYAGE 2, 88.6% of patients receiving guselkumab maintenance treatment at Week 48 were PASI 90 responders compared to 36.8% of patients who were withdrawn from treatment at Week 28 ( $p < 0.001$ ). Loss of PASI 90 response was noted as early as 4 weeks after withdrawal of guselkumab treatment with a median time to loss of PASI 90 response of approximately 15 weeks. Among patients who were withdrawn from treatment and subsequently re-initiated guselkumab, 80% regained a PASI 90 response when assessed 20 weeks after initiation of retreatment.

In VOYAGE 2, among 112 patients randomised to adalimumab who failed to achieve a PASI 90 response at Week 28, 66% and 76% achieved a PASI 90 response after 20 and 44 weeks of treatment with guselkumab, respectively. In addition, among 95 patients randomised to guselkumab who failed to achieve a PASI 90 response at Week 28, 36% and 41% achieved a PASI 90 response with an additional 20 and 44 weeks of continued treatment with guselkumab, respectively. No new safety findings were observed in patients who switched from adalimumab to guselkumab.

### Regional disease

In VOYAGE 1 and 2, significant improvements were seen in scalp, hand and foot, and nail psoriasis (as measured by the Scalp-specific Investigator Global Assessment [ss-IGA], Physician's Global Assessment of Hands and/or Feet [hf-PGA], Fingernail Physician's Global Assessment [f-PGA] and Nail Psoriasis Severity Index [NAPSI], respectively) in guselkumab treated patients compared to placebo treated patients at Week 16 ( $p < 0.001$ , Table 4). Guselkumab demonstrated superiority compared to adalimumab for scalp and hand and foot psoriasis at Week 24 (VOYAGE 1 and 2) and Week 48 (VOYAGE 1) ( $p \leq 0.001$ , except for hand and foot psoriasis at Week 24 [VOYAGE 2] and Week 48 [VOYAGE 1],  $p < 0.05$ ).

**Table 4: Summary of Regional Disease Responses in VOYAGE 1 and VOYAGE 2**

	VOYAGE 1			VOYAGE 2		
	Placebo	Guselkumab	Adalimumab	Placebo	Guselkumab	Adalimumab
<b>ss-IGA (N)<sup>a</sup></b>	145	277	286	202	408	194
ss-IGA 0/1 <sup>b</sup> , n (%)						
Week 16	21 (14.5)	231 (83.4) <sup>c</sup>	201 (70.3) <sup>d</sup>	22 (10.9)	329 (80.6) <sup>c</sup>	130 (67.0) <sup>d</sup>
<b>hf-PGA (N)<sup>a</sup></b>	43	90	95	63	114	56
hf-PGA 0/1 <sup>b</sup> , n (%)						
Week 16	6 (14.0)	66 (73.3) <sup>c</sup>	53 (55.8) <sup>d</sup>	9 (14.3)	88 (77.2) <sup>c</sup>	40 (71.4) <sup>d</sup>
<b>f-PGA (N)<sup>a</sup></b>	88	174	173	123	246	124
f-PGA 0/1, n (%)						
Week 16	14 (15.9)	68 (39.1) <sup>c</sup>	88 (50.9) <sup>d</sup>	18 (14.6)	128 (52.0) <sup>c</sup>	74 (59.7) <sup>d</sup>
<b>NAPSI (N)<sup>a</sup></b>	99	194	191	140	280	140
Percent Improvement, mean (SD)						
Week 16	-0.9 (57.9)	34.4 (42.4) <sup>c</sup>	38.0 (53.9) <sup>d</sup>	1.8 (53.8)	39.6 (45.6) <sup>c</sup>	46.9 (48.1) <sup>d</sup>

<sup>a</sup> Includes only subjects with ss-IGA, f-PGA, hf-PGA score  $\geq 2$  at baseline or baseline NAPSI score  $> 0$ .

<sup>b</sup> Includes only subjects achieving  $\geq 2$ -grade improvement from baseline in ss-IGA and/or hf-PGA.

<sup>c</sup>  $p < 0.001$  for comparison between guselkumab and placebo for the major secondary endpoint.

<sup>d</sup> comparisons between guselkumab and adalimumab were not performed.

<sup>e</sup>  $p < 0.001$  for comparison between guselkumab and placebo.

### Health-related quality of life / Patient reported outcomes

Across VOYAGE 1 and 2 significantly greater improvements in health-related quality of life as measured by Dermatology Life Quality Index (DLQI) and in patient-reported psoriasis symptoms (itching, pain, burning, stinging and skin tightness) and signs (skin dryness, cracking, scaling, shedding or flaking, redness and bleeding) as measured by the Psoriasis Symptoms and Signs Diary (PSSD) were observed in guselkumab patients compared to placebo patients at Week 16 (Table 5). Signs of improvement on patient-reported outcomes were maintained through Week 24 (VOYAGE 1 and 2) and Week 48 (VOYAGE 1). In VOYAGE 1, for patients receiving continuous guselkumab treatment, these improvements were maintained in the open-label phase through Week 156 (Table 6).

**Table 5: Summary of Patient Reported Outcomes at Week 16 in VOYAGE 1 and VOYAGE 2**

	VOYAGE 1			VOYAGE 2		
	Placebo	Guselkumab	Adalimumab	Placebo	Guselkumab	Adalimumab
<b>DLQI</b> , subjects with baseline score	170	322	328	248	495	247
Change from baseline, mean (standard deviation)						
Week 16	-0.6 (6.4)	-11.2 (7.2) <sup>c</sup>	-9.3 (7.8) <sup>b</sup>	-2.6 (6.9)	-11.3 (6.8) <sup>c</sup>	-9.7 (6.8) <sup>b</sup>
<b>PSSD Symptom score</b> , subjects with baseline score > 0	129	248	273	198	410	200
Symptom score = 0, n (%)						
Week 16	1 (0.8)	67 (27.0) <sup>a</sup>	45 (16.5) <sup>b</sup>	0	112 (27.3) <sup>a</sup>	30 (15.0) <sup>b</sup>
<b>PSSD Sign score</b> , subjects with baseline score > 0	129	248	274	198	411	201
Sign score = 0, n (%)						
Week 16	0	50 (20.2) <sup>a</sup>	32 (11.7) <sup>b</sup>	0	86 (20.9) <sup>a</sup>	21 (10.4) <sup>b</sup>

<sup>a</sup> p < 0.001 for comparison between guselkumab and placebo.

<sup>b</sup> comparisons between guselkumab and adalimumab were not performed.

<sup>c</sup> p < 0.001 for comparison between guselkumab and placebo for major secondary endpoints.

**Table 6: Summary of Patient Reported Outcomes in the Open-Label Phase in VOYAGE 1**

	Guselkumab		Adalimumab-Guselkumab	
	Week 76	Week 156	Week 76	Week 156
<b>DLQI</b> score > 1 at baseline, n	445	411	264	251
Subjects with DLQI 0/1	337 (75.7%)	307 (74.7%)	198 (75.0%)	190 (75.7%)
<b>PSSD Symptom Score</b> , subjects with baseline score > 0	347	319	227	214
Symptom score = 0, n (%)	136 (39.2%)	129 (40.4%)	99 (43.6%)	96 (44.9%)
<b>PSSD Sign score</b> , subjects with baseline score > 0	347	319	228	215
Sign score = 0, n (%)	102 (29.4%)	93 (29.2%)	71 (31.1%)	69 (32.1%)

In VOYAGE 2, guselkumab patients had significantly greater improvement from baseline compared to placebo in health-related quality of life, anxiety and depression, and work limitation measures at Week 16, as measured by the 36-item Short Form (SF-36) health survey questionnaire, Hospital Anxiety and Depression Scale (HADS), and Work Limitations Questionnaire (WLQ), respectively. The improvements in SF-36, HADS and WLQ were all maintained through Week 48 and in the open-label phase through Week 156 among patients randomised to maintenance therapy at Week 28.

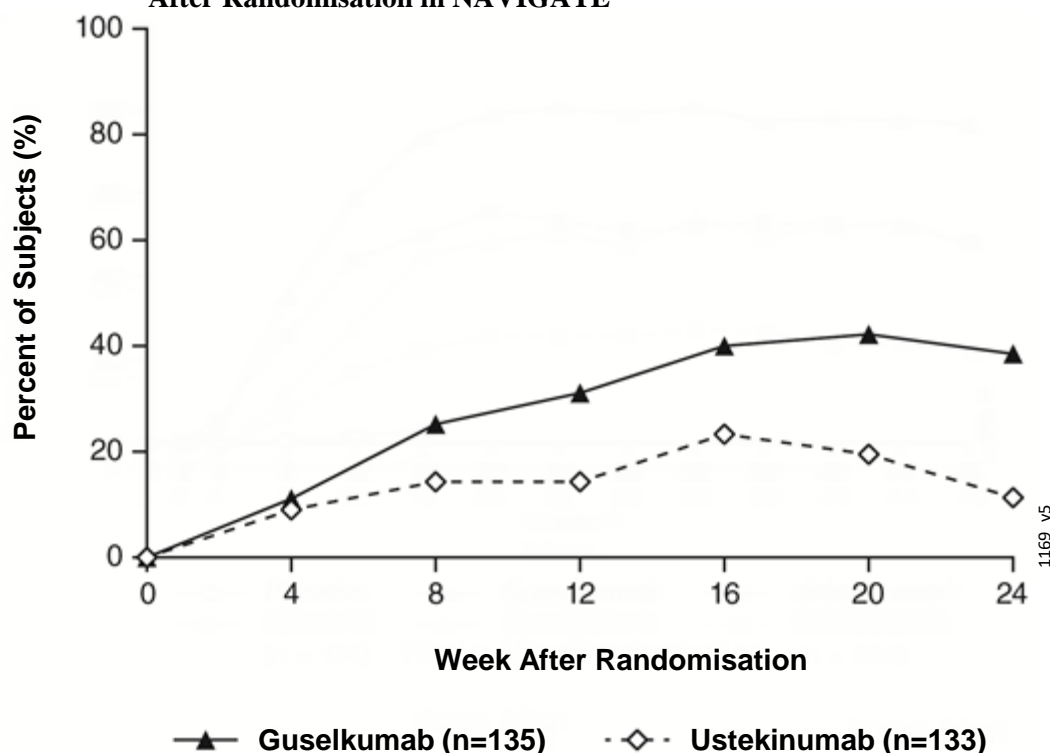
### NAVIGATE

The NAVIGATE study examined the efficacy of guselkumab in patients who had an inadequate response (ie, who had not achieved a 'cleared' or 'minimal' response defined as IGA  $\geq 2$ ) to ustekinumab at Week 16. All patients (N=871) received open-label ustekinumab (45 mg  $\leq 100$  kg and 90 mg  $> 100$  kg) at Weeks 0 and 4. At Week 16, 268 patients with an IGA  $\geq 2$  score were randomised to either continue ustekinumab treatment (N=133) q12w, or to initiate guselkumab treatment (N=135) at Weeks 16, 20, and q8w thereafter. Baseline characteristics for randomised patients were similar to those observed in VOYAGE 1 and 2.

After randomisation, the primary endpoint was the number of post-randomisation visits between Weeks 12 and 24 at which patients achieved an IGA score 0/1 and had  $\geq 2$  grade improvement. Patients were examined at four week intervals for a total of four visits. Among patients who inadequately responded to ustekinumab at the time of randomisation, significantly greater improvement of efficacy was observed in patients who switched to guselkumab treatment compared to patients who continued ustekinumab treatment. Between 12 and 24 weeks after randomisation, guselkumab patients achieved an IGA score 0/1 with  $\geq 2$  grade improvement twice as often as ustekinumab patients (mean 1.5 vs 0.7 visits, respectively, p < 0.001). Additionally, at 12 weeks after randomisation a higher proportion of guselkumab patients compared to ustekinumab patients achieved

an IGA score 0/1 and  $\geq 2$  grade improvement (31.1% vs. 14.3%, respectively;  $p = 0.001$ ) and a PASI 90 response (48% vs 23%, respectively,  $p < 0.001$ ). Differences in response rates between guselkumab and ustekinumab treated patients were noted as early as 4 weeks after randomisation (11.1% and 9.0%, respectively) and reached a maximum 24 weeks after randomisation (see Figure 3). No new safety findings were observed in patients who switched from ustekinumab to guselkumab.

**Figure 3: Percent of Subjects Who Achieved an IGA Score of Cleared (0) or Minimal (1) and at least a 2-grade improvement in IGA from Week 0 Through Week 24 by Visit After Randomisation in NAVIGATE**



#### ECLIPSE

Efficacy and safety of guselkumab were also investigated in a double-blind study compared to secukinumab. Patients were randomised to receive guselkumab (N=534; 100 mg at Week 0, 4 and q8w thereafter), or secukinumab (N=514; 300 mg at Week 0, 1, 2, 3, 4, and q4w thereafter). The last dose was at week 44 for both treatment groups.

Baseline disease characteristics were consistent with a population of moderate to severe plaque psoriasis with a median BSA of 20%, a median PASI score of 18, and an IGA score of severe for 24% of patients.

Guselkumab was superior to secukinumab as measured by the primary endpoint of PASI 90 response at Week 48 (84.5% versus 70.0%,  $p < 0.001$ ). Comparative PASI response rates are presented in Table 7.

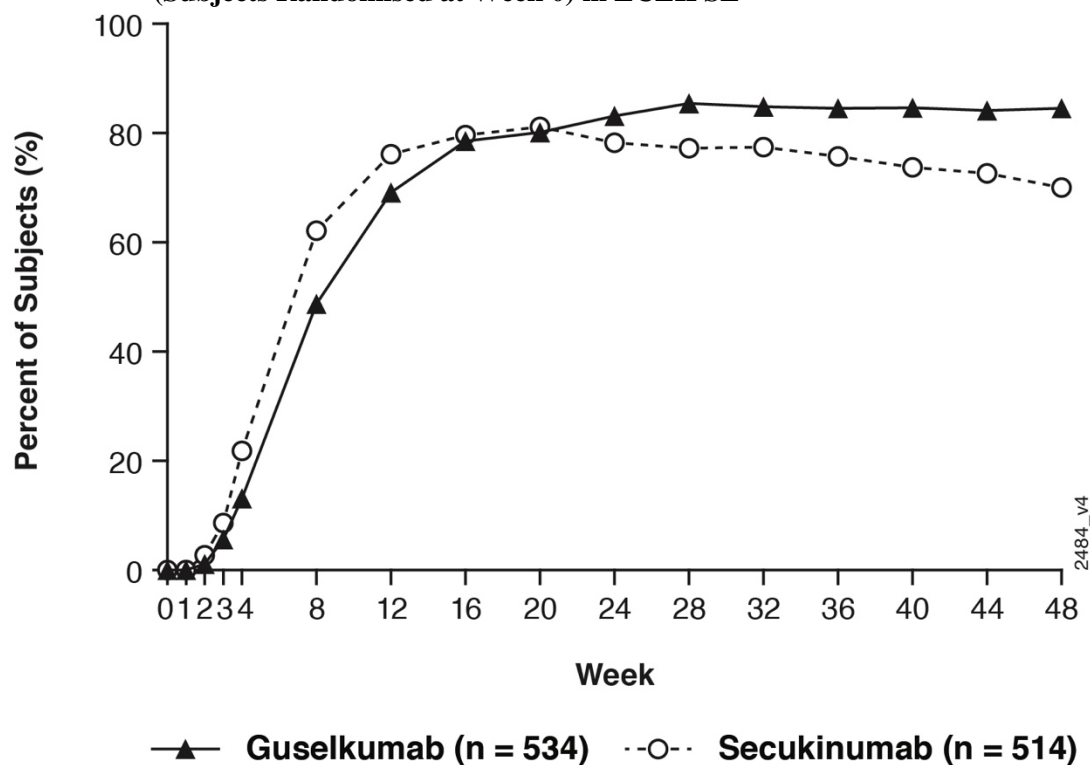
**Table 7: PASI Response Rates in ECLIPSE**

	Number of patients (%)	
	Guselkumab (N=534)	Secukinumab (N=514)
<b>Primary Endpoint</b>		
PASI 90 response at Week 48	451 (84.5%) <sup>a</sup>	360 (70.0%)
<b>Major Secondary Endpoints</b>		
PASI 75 response at both Week 12 and Week 48	452 (84.6%) <sup>b</sup>	412 (80.2%)
PASI 75 response at Week 12	477 (89.3%) <sup>c</sup>	471 (91.6%)
PASI 90 response at Week 12	369 (69.1%) <sup>c</sup>	391 (76.1%)
PASI 100 response at Week 48	311 (58.2%) <sup>c</sup>	249 (48.4%)

- <sup>a</sup>  $p < 0.001$  for superiority  
<sup>b</sup>  $p < 0.001$  for non-inferiority,  $p=0.062$  for superiority  
<sup>c</sup> formal statistical testing was not performed

Guselkumab and secukinumab PASI 90 response rates through Week 48 are presented in Figure 4.

**Figure 4: Percent of Subjects Who Achieved a PASI 90 Response Through Week 48 by Visit (Subjects Randomised at Week 0) in ECLIPSE**



#### Psoriatic arthritis (PsA)

Guselkumab has been shown to improve signs and symptoms, physical function and health-related quality of life, and reduce the rate of progression of peripheral joint damage in adult patients with active PsA.

#### *DISCOVER 1 and DISCOVER 2*

Two randomised, double-blind, placebo-controlled phase III studies (DISCOVER 1 and DISCOVER 2) evaluated the efficacy and safety of guselkumab versus placebo in adult patients with active PsA ( $\geq 3$  swollen and  $\geq 3$  tender joints, and a C-reactive protein (CRP) level of  $\geq 0.3$  mg/dL in DISCOVER 1, and  $\geq 5$  swollen and  $\geq 5$  tender joints, and a CRP level of  $\geq 0.6$  mg/dL in DISCOVER 2), despite conventional synthetic (cs)DMARD, apremilast, or nonsteroidal anti-inflammatory drug (NSAID) therapy. Patients in these studies had a diagnosis of PsA based on the Classification criteria for Psoriatic Arthritis [CASPAR] for a median duration of 4 years. Patients with different subtypes of PsA 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%). Over 65% and 42% of the patients had enthesitis and dactylitis at baseline, respectively, and over 75% of patients had  $\geq 3\%$  BSA psoriasis skin involvement. DISCOVER 1 and DISCOVER 2 evaluated 381 and 739 patients, respectively, who received treatment with guselkumab 100 mg administered at Weeks 0 and 4 followed by every 8 weeks (q8w) or guselkumab 100 mg q4w, or placebo. Approximately 58% of patients in both studies continued on stable doses of MTX ( $\leq 25$  mg/week).

In both studies over 90% of patients had prior csDMARD use. In DISCOVER 1, 31% of patients had previously received anti-TNF $\alpha$  treatment. In DISCOVER 2, all patients were naive to biologic therapy.

### Signs and symptoms

Treatment with guselkumab resulted in significant improvements in the measures of disease activity compared to placebo at Week 24. The primary endpoint in both studies was the percentage of patients who achieved American College of Rheumatology (ACR) 20 response at Week 24. The key efficacy results are shown in Table 8.

**Table 8: Clinical Responses in DISCOVER 1 and DISCOVER 2**

	Placebo (N=126)	DISCOVER 1		Placebo (N=246)	DISCOVER 2	
		100 mg q8w (N=127)	100 mg q4w (N=128)		100 mg q8w (N=248)	100 mg q4w (N=245)
<b>ACR 20 response</b>						
Week 16	25.4%	52.0% <sup>b</sup>	60.2% <sup>b</sup>	33.7%	55.2% <sup>g</sup>	55.9% <sup>c</sup>
Difference from placebo (95% CI)	-	26.7 (15.3, 38.1)	34.8 (23.5, 46.0)	-	21.5 (13.1, 30.0)	22.2 (13.7, 30.7)
Week 24	22.2%	52.0% <sup>a</sup>	59.4% <sup>a</sup>	32.9%	64.1% <sup>a</sup>	63.7% <sup>a</sup>
Difference from placebo (95% CI)	-	29.8 (18.6, 41.1)	37.1 (26.1, 48.2)	-	31.2 (22.9, 39.5)	30.8 (22.4, 39.1)
<b>ACR 50 response</b>						
Week 16	12.7%	22.8% <sup>d</sup>	26.6% <sup>c</sup>	9.3%	28.6% <sup>g</sup>	20.8% <sup>c</sup>
Difference from placebo (95% CI)	-	10.2 (1.0, 19.3)	13.9 (4.4, 23.4)	-	19.3 (12.6, 25.9)	11.5 (5.2, 17.7)
Week 24	8.7%	29.9% <sup>b</sup>	35.9% <sup>b</sup>	14.2%	31.5% <sup>g</sup>	33.1% <sup>c</sup>
Difference from placebo (95% CI)	-	21.4 (12.1, 30.7)	27.2 (17.6, 36.8)	-	17.2 (10.0, 24.4)	18.8 (11.5, 26.1)
<b>ACR 70 response</b>						
Week 24	5.6%	11.8% <sup>d</sup>	20.3% <sup>b</sup>	4.1%	18.5% <sup>g</sup>	13.1% <sup>c</sup>
Difference from placebo (95% CI)	-	6.4 (-0.3, 13.1)	14.8 (6.9, 22.7)	-	14.5 (9.1, 19.9)	9.0 (4.1, 13.8)
<b>DAS (CRP) change from baseline</b>						
Week 24 <sup>c</sup>	-0.70	-1.43 <sup>b</sup>	-1.61 <sup>b</sup>	-0.97	-1.59 <sup>b</sup>	-1.62 <sup>b</sup>
Difference from placebo (95% CI)	-	-0.73 (-0.98, -0.48)	-0.91 (-1.16, -0.66)	-	-0.61 (-0.80, -0.43)	-0.65 (-0.83, -0.47)
<b>Minimal Disease Activity</b>						
Week 24	11.1%	22.8% <sup>f</sup>	30.5% <sup>e</sup>	6.1%	25.0% <sup>e</sup>	18.8% <sup>e</sup>
Difference from placebo (95% CI)	-	11.9 (2.9, 20.9)	19.3 (9.7, 28.9)	-	18.9 (12.8, 25.0)	12.7 (7.0, 18.4)
<b>Patients with <math>\geq 3\%</math> BSA and IGA <math>\geq 2</math></b>						
	n=78	n=82	n=89	n=183	n=176	n=184
<b>IGA response<sup>h</sup></b>						
Week 24	15.4%	57.3% <sup>b</sup>	75.3% <sup>b</sup>	19.1%	70.5% <sup>b</sup>	68.5% <sup>b</sup>
Difference from placebo (95% CI)	-	42.0 (28.9, 55.1)	60.0 (48.3, 71.8)	-	50.9 (42.2, 59.7)	49.8 (41.2, 58.4)
<b>PASI 90 response</b>						
Week 16	10.3%	45.1% <sup>e</sup>	52.8% <sup>e</sup>	8.2%	55.1% <sup>e</sup>	53.8% <sup>e</sup>
Difference from placebo (95% CI)	-	34.9 (22.2, 47.6)	42.6 (30.5, 54.8)	-	46.6 (38.4, 54.8)	45.6 (37.6, 53.6)
Week 24	11.5%	50.0% <sup>e</sup>	62.9% <sup>e</sup>	9.8%	68.8% <sup>e</sup>	60.9% <sup>e</sup>
Difference from placebo (95% CI)	-	38.6 (25.8, 51.4)	51.7 (39.7, 63.7)	-	58.6 (50.6, 66.6)	51.3 (43.2, 59.3)

<sup>a</sup> p < 0.001 (primary endpoint)

<sup>b</sup> p < 0.001 (major secondary endpoint)

<sup>c</sup> p = 0.006 (major secondary endpoint)

<sup>d</sup> not statistically significant p=0.086 (major secondary endpoint)

<sup>e</sup> nominal p < 0.001

<sup>f</sup> nominal p = 0.012

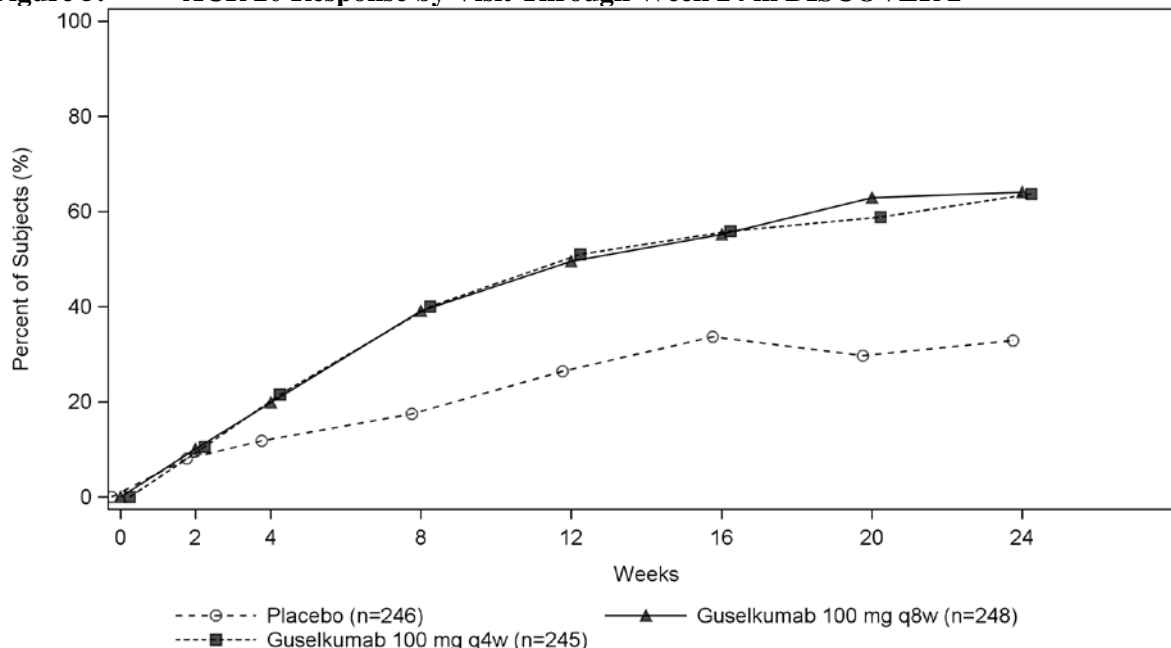
<sup>g</sup> not formally tested in the hierarchical testing procedure, nominal p < 0.001 (major secondary endpoint)

<sup>h</sup> defined as a IGA response of 0 (cleared) or 1 (minimal) and  $\geq 2$ -grade reduction from baseline in the IGA psoriasis score

### Response over time

In DISCOVER 2, a greater ACR 20 response was observed in both guselkumab groups compared to placebo as early as Week 4 and the treatment difference continued to increase over time through Week 24 (Figure 5).

**Figure 5: ACR 20 Response by Visit Through Week 24 in DISCOVER 2**



Responses observed in the guselkumab groups were similar regardless of concomitant csDMARD use, including MTX (DISCOVER 1 and 2). Additionally, examination of age, gender, race, body weight, and previous csDMARD use (DISCOVER 1 and 2) and previous anti-TNF $\alpha$  use (DISCOVER 1), did not identify differences in response to guselkumab among these subgroups.

In DISCOVER 1 and 2, improvements were shown in all components of the ACR scores including patient assessment of pain. At Week 24 in both studies, the proportion of patients achieving a modified PsA response criteria (PsARC) response was greater in the guselkumab groups compared to placebo.

Dactylitis and enthesitis were assessed based on pooled data from DISCOVER 1 and 2. At Week 24, among patients with dactylitis at baseline, the proportion of subjects with dactylitis resolution was greater in the guselkumab q8w group (59.4%, nominal  $p < 0.001$ ) and q4w group (63.5%,  $p = 0.006$ ) compared to placebo (42.2%). At Week 24, among patients with enthesitis at baseline, the proportion of subjects with enthesitis resolution was greater in the guselkumab q8w group (49.6%, nominal  $p < 0.001$ ) and q4w group (44.9%,  $p = 0.006$ ) compared to placebo (29.4%).

In DISCOVER 1 and 2, patients treated with guselkumab who had spondylitis with peripheral arthritis as their primary presentation, demonstrated greater improvement from baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) compared to placebo at Week 24.

### 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 guselkumab q4w group demonstrated statistically significantly less radiographic progression and the guselkumab q8w group showed numerically less progression than placebo (Table 9). The observed benefit with the guselkumab q4w dosing regimen on inhibition of radiographic progression (ie, smaller mean change from baseline in total modified vdH-S score in the q4w group versus placebo) was most pronounced in subjects with both a high C-reactive protein value and high number of joints with erosions at baseline.



<b>Table 9: Change from baseline in total modified vdH-S score at Week 24 in DISCOVER 2</b>		
	N	LSMean change <sup>c</sup> (95% CI <sup>d</sup> ) from baseline in modified vdH-S score at Week 24
Placebo	246	0.95 (0.61, 1.29)
Guselkumab 100 mg q8w	248	0.52 <sup>a</sup> (0.18, 0.86)
Guselkumab 100 mg q4w	245	0.29 <sup>b</sup> (-0.05, 0.63)

<sup>a</sup> not statistically significant p = 0.068 (major secondary endpoint)

<sup>b</sup> p = 0.006 (major secondary endpoint)

<sup>c</sup> LSmean change = least squares mean change

<sup>d</sup> CI = confidence interval

At Week 52, the mean change from baseline in total modified vdH-S was similar in the guselkumab q8w and q4w groups (Table 10).

<b>Table 10: Change from baseline in total modified vdH-S score at Week 52 in DISCOVER 2</b>		
	N	Mean change <sup>a</sup> (SD <sup>b</sup> ) from baseline in total modified vdH-S score at Week 52
Guselkumab 100 mg q8w	235	0.97 (3.623)
Guselkumab 100 mg q4w	229	1.07 (3.843)

<sup>a</sup> Based on observed data at Week 52

<sup>b</sup> SD = standard deviation

Note: no placebo group beyond Week 24

### Physical function and health-related quality of life

In DISCOVER 1 and 2, guselkumab treated patients showed significant improvement (p < 0.001) in physical function compared to placebo as assessed by the Health Assessment Questionnaire-Disability Index (HAQ-DI) at Week 24.

A significantly greater improvement from baseline in the SF-36 Physical Component Summary score was observed in guselkumab treated patients compared to placebo at Week 24 in DISCOVER 1 (p < 0.001 for both dose groups) and DISCOVER 2 (p = 0.006 for q4w group). At Week 24, a greater increase from baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) score was observed in guselkumab treated patients compared to placebo in both studies. In DISCOVER 2, greater improvements in health-related quality of life as measured by the Dermatology Life Quality Index (DLQI) were observed in guselkumab treated patients compared to placebo at Week 24.

### Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Tremfya in plaque psoriasis and psoriatic arthritis in one or more subsets of the paediatric population (see section 4.2 for information on paediatric use).

## **5.2 Pharmacokinetic properties**

### Absorption

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

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

The pharmacokinetics of guselkumab in subjects with psoriatic arthritis was similar to that in subjects with psoriasis. Following subcutaneous administration of 100 mg of Tremfya at Weeks 0, 4, and every 8 weeks thereafter, mean steady-state trough serum guselkumab concentration was also approximately 1.2 mcg/mL. Following subcutaneous administration of 100 mg of Tremfya every 4 weeks, mean steady-state trough serum guselkumab concentration was approximately 3.8 mcg/mL.

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

#### Distribution

Mean volume of distribution during the terminal phase ( $V_z$ ) following a single intravenous administration to healthy subjects ranged from approximately 7 to 10 L across studies.

#### Biotransformation

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

#### Elimination

Mean systemic clearance (CL) following a single intravenous administration to healthy subjects ranged from 0.288 to 0.479 L/day across studies. Mean half-life ( $T_{1/2}$ ) of guselkumab was approximately 17 days in healthy subjects and approximately 15 to 18 days in patients with plaque psoriasis across studies.

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

#### Linearity/non-linearity

The systemic exposure of guselkumab ( $C_{max}$  and AUC) increased in an approximately dose-proportional manner following a single subcutaneous injection at doses ranging from 10 mg to 300 mg in healthy subjects or patients with plaque psoriasis.

#### Elderly patients

No specific studies have been conducted in elderly patients. Of the 1384 plaque psoriasis patients exposed to guselkumab in phase III clinical studies and included in the population pharmacokinetic analysis, 70 patients were 65 years of age or older, including 4 patients who were 75 years of age or older. Of the 746 psoriatic arthritis patients exposed to guselkumab in phase III clinical studies, a total of 38 patients were 65 years of age or older, and no patients were 75 years of age or older.

Population pharmacokinetic analyses in plaque psoriasis and psoriatic arthritis patients indicated no apparent changes in CL/F estimate in patients  $\geq 65$  years of age compared to patients  $< 65$  years of age, suggesting no dose adjustment is needed for elderly patients.

#### Patients with renal or hepatic impairment

No specific study has been conducted to determine the effect of renal or hepatic impairment on the pharmacokinetics of guselkumab. Renal elimination of intact guselkumab, an IgG mAb, is expected to be low and of minor importance; similarly, hepatic impairment is not expected to influence clearance of guselkumab as IgG mAbs are mainly eliminated via intracellular catabolism.

### **5.3 Preclinical safety data**

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeat-dose toxicity, toxicity to reproduction and pre- and post-natal development.

In repeat-dose toxicity studies in cynomolgus monkeys, guselkumab was well tolerated via intravenous and subcutaneous routes of administration. A weekly subcutaneous dose of 50 mg/kg to monkeys resulted in exposure (AUC) and  $C_{max}$  values that were at least 49-fold and  $>200$ -fold higher, respectively, than those measured in the human clinical PK study. Additionally, there were no adverse immunotoxicity or cardiovascular safety pharmacology effects noted during the conduct of the repeat-dose toxicity studies or in a targeted cardiovascular safety pharmacology study in cynomolgus monkeys.

There were no preneoplastic changes observed in histopathology evaluations of animals treated up to

24-weeks, or following the 12-week recovery period during which drug was detectable in the serum.

No mutagenicity or carcinogenicity studies were conducted with guselkumab.

Guselkumab could not be detected in breast milk from cynomolgus monkeys as measured at post-natal day 28.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Histidine  
Histidine monohydrochloride monohydrate  
Polysorbate 80  
Sucrose  
Water for injections

### **6.2 Incompatibilities**

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

### **6.3 Shelf life**

2 years.

### **6.4 Special precautions for storage**

Store in a refrigerator (2°C–8°C). Do not freeze.  
Keep the pre-filled syringe or pre-filled pen in the outer carton in order to protect from light.

### **6.5 Nature and contents of container**

#### Tremfya 100 mg solution for injection in pre-filled syringe

1 mL solution in a pre-filled glass syringe with a fixed needle and a needle shield, assembled in an automatic needle guard.

Tremfya is available in a pack containing one pre-filled syringe and in a multipack containing 2 (2 packs of 1) pre-filled syringes.

Not all pack sizes may be marketed.

#### Tremfya 100 mg solution for injection in pre-filled pen

1 mL solution in a pre-filled glass syringe assembled in a pre-filled pen with an automatic needle guard.

Tremfya is available in a pack containing one pre-filled pen and in a multipack containing 2 (2 packs of 1) pre-filled pens.

Not all pack sizes may be marketed.

### **6.6 Special precautions for disposal and other handling**

After removing the pre-filled syringe or pre-filled pen from the refrigerator, keep the pre-filled syringe or pre-filled pen inside the carton and allow to reach room temperature by waiting for 30 minutes before injecting Tremfya. The pre-filled syringe or pre-filled pen should not be shaken.

Prior to use, a visual inspection of the pre-filled syringe or pre-filled pen is recommended. The solution should be clear, colourless to light yellow, and may contain a few small white or clear particles. Tremfya should not be used if the solution is cloudy or discoloured, or contains large particles.

Each Tremfya pack is provided with an 'Instructions for use' leaflet that fully describes the preparation and administration of the pre-filled syringe or pre-filled pen.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

## **7. MARKETING AUTHORISATION HOLDER**

Janssen-Cilag International NV  
Turnhoutseweg 30  
B-2340 Beerse  
Belgium

## **8. MARKETING AUTHORISATION NUMBER(S)**

EU/1/17/1234/001 1 pre-filled syringe  
EU/1/17/1234/002 1 pre-filled pen  
EU/1/17/1234/003 2 pre-filled pens  
EU/1/17/1234/004 2 pre-filled syringes

## **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 10 November 2017

## **10. DATE OF REVISION OF THE TEXT**

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu/>

## **ANNEX II**

- A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE  
SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR  
BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY  
AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE  
MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE  
SAFE AND EFFECTIVE USE OF THE MEDICINAL  
PRODUCT**

**A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturers of the biological active substance

Biogen Inc. (BIIB)  
5000 Davis Drive  
Research Triangle Park  
NC27709  
USA

Janssen Sciences Ireland UC  
Barnahely  
Ringaskiddy  
Co. Cork  
Ireland

Name and address of the manufacturer responsible for batch release

Janssen Biologics B.V.  
Einsteinweg 101  
2333CB Leiden  
The Netherlands

**B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

**C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

**D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**



**PARTICULARS TO APPEAR ON THE OUTER PACKAGING****PRE-FILLED SYRINGE CARTON TEXT (100 mg)****1. NAME OF THE MEDICINAL PRODUCT**

Tremfya 100 mg solution for injection in pre-filled syringe  
guselkumab

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each pre-filled syringe contains 100 mg of guselkumab in 1 mL.

**3. LIST OF EXCIPIENTS**

Excipients: sucrose, histidine, histidine monohydrochloride monohydrate, polysorbate 80, water for injections.

**4. PHARMACEUTICAL FORM AND CONTENTS**

Solution for injection

1 pre-filled syringe

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Do not shake  
Subcutaneous use  
Read the package leaflet before use.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY****8. EXPIRY DATE**

EXP

**9. SPECIAL STORAGE CONDITIONS**

Store in a refrigerator.  
Do not freeze.

Keep the pre-filled syringe in the outer carton in order to protect from light.

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Janssen-Cilag International NV  
Turnhoutseweg 30  
B-2340 Beerse  
Belgium

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/17/1234/001

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY**

**15. INSTRUCTIONS ON USE**

**16. INFORMATION IN BRAILLE**

Tremfya 100 mg

**17. UNIQUE IDENTIFIER – 2D BARCODE**

2D barcode carrying the unique identifier included.

**18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

PC  
SN  
NN

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING****CARTON FOR 1 PRE-FILLED SYRINGE (100 mg) AS INTERMEDIATE PACK /  
COMPONENT OF A MULTIPACK (WITHOUT BLUE BOX)****1. NAME OF THE MEDICINAL PRODUCT**

Tremfya 100 mg solution for injection in pre-filled syringe  
guselkumab

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each pre-filled syringe contains 100 mg of guselkumab in 1 mL.

**3. LIST OF EXCIPIENTS**

Excipients: sucrose, histidine, histidine monohydrochloride monohydrate, polysorbate 80, water for injections.

**4. PHARMACEUTICAL FORM AND CONTENTS**

Solution for injection

1 pre-filled syringe  
Component of a multipack, cannot be sold separately

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Do not shake  
Subcutaneous use  
Read the package leaflet before use.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT  
OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY****8. EXPIRY DATE**

EXP

**9. SPECIAL STORAGE CONDITIONS**

Store in a refrigerator.

Do not freeze.

Keep the pre-filled syringe in the outer carton in order to protect from light.

<b>10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE</b>
--

<b>11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER</b>
---

Janssen-Cilag International NV  
Turnhoutseweg 30  
B-2340 Beerse  
Belgium

<b>12. MARKETING AUTHORISATION NUMBER(S)</b>
--

EU/1/17/1234/004

<b>13. BATCH NUMBER</b>
-------------------------

Lot

<b>14. GENERAL CLASSIFICATION FOR SUPPLY</b>
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<b>15. INSTRUCTIONS ON USE</b>
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<b>16. INFORMATION IN BRAILLE</b>
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Tremfya 100 mg

<b>17. UNIQUE IDENTIFIER – 2D BARCODE</b>
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<b>18. UNIQUE IDENTIFIER - HUMAN READABLE DATA</b>
--

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**CARTON FOR PRE-FILLED SYRINGE MULTIPACK COMPRISING 2 PACKS  
(INCLUDING BLUE BOX)**

**1. NAME OF THE MEDICINAL PRODUCT**

Tremfya 100 mg solution for injection in pre-filled syringe  
guselkumab

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each pre-filled syringe contains 100 mg of guselkumab in 1 mL.

**3. LIST OF EXCIPIENTS**

Excipients: sucrose, histidine, histidine monohydrochloride monohydrate, polysorbate 80, water for injections.

**4. PHARMACEUTICAL FORM AND CONTENTS**

Solution for injection

Multipack: 2 (2 packs of 1) pre-filled syringes

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Do not shake  
Subcutaneous use  
Read the package leaflet before use.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT  
OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY**

**8. EXPIRY DATE**

EXP

**9. SPECIAL STORAGE CONDITIONS**

Store in a refrigerator.  
Do not freeze.

Keep the pre-filled syringe in the outer carton in order to protect from light.

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Janssen-Cilag International NV  
Turnhoutseweg 30  
B-2340 Beerse  
Belgium

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/17/1234/004 (2 packs, each containing 1 pre-filled syringe)

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY**

**15. INSTRUCTIONS ON USE**

**16. INFORMATION IN BRAILLE**

Tremfya 100 mg

**17. UNIQUE IDENTIFIER – 2D BARCODE**

2D barcode carrying the unique identifier included.

**18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

PC  
SN  
NN

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**PRE-FILLED SYRINGE LABEL TEXT (100 mg)**

**1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION**

Tremfya 100 mg  
injection  
guselkumab  
SC

**2. METHOD OF ADMINISTRATION**

**3. EXPIRY DATE**

EXP

**4. BATCH NUMBER**

Lot

**5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT**

1 mL

**6. OTHER**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING****PRE-FILLED PEN CARTON TEXT (100 mg)****1. NAME OF THE MEDICINAL PRODUCT**

Tremfya 100 mg solution for injection in pre-filled pen  
guselkumab

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each pre-filled pen contains 100 mg of guselkumab in 1 mL.

**3. LIST OF EXCIPIENTS**

Excipients: sucrose, histidine, histidine monohydrochloride monohydrate, polysorbate 80, water for injections.

**4. PHARMACEUTICAL FORM AND CONTENTS**

Solution for injection

1 pre-filled pen

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Do not shake  
Subcutaneous use  
Read the package leaflet before use.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY****8. EXPIRY DATE**

EXP

**9. SPECIAL STORAGE CONDITIONS**

Store in a refrigerator.  
Do not freeze.



Keep the pre-filled pen in the outer carton in order to protect from light.

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Janssen-Cilag International NV  
Turnhoutseweg 30  
B-2340 Beerse  
Belgium

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/17/1234/002

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY**

**15. INSTRUCTIONS ON USE**

**16. INFORMATION IN BRAILLE**

Tremfya 100 mg

**17. UNIQUE IDENTIFIER – 2D BARCODE**

2D barcode carrying the unique identifier included.

**18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

PC  
SN  
NN

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING****CARTON FOR 1 PRE-FILLED PEN (100 mg) AS INTERMEDIATE PACK / COMPONENT OF A MULTIPACK (WITHOUT BLUE BOX)****1. NAME OF THE MEDICINAL PRODUCT**

Tremfya 100 mg solution for injection in pre-filled pen  
guselkumab

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each pre-filled pen contains 100 mg of guselkumab in 1 mL.

**3. LIST OF EXCIPIENTS**

Excipients: sucrose, histidine, histidine monohydrochloride monohydrate, polysorbate 80, water for injections.

**4. PHARMACEUTICAL FORM AND CONTENTS**

Solution for injection

1 pre-filled pen  
Component of a multipack, cannot be sold separately

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Do not shake  
Subcutaneous use  
Read the package leaflet before use.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY****8. EXPIRY DATE**

EXP

**9. SPECIAL STORAGE CONDITIONS**

Store in a refrigerator.  
Do not freeze.

Keep the pre-filled pen in the outer carton in order to protect from light.

<b>10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE</b>
--

<b>11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER</b>
---

Janssen-Cilag International NV  
Turnhoutseweg 30  
B-2340 Beerse  
Belgium

<b>12. MARKETING AUTHORISATION NUMBER(S)</b>
--

EU/1/17/1234/003

<b>13. BATCH NUMBER</b>
-------------------------

Lot

<b>14. GENERAL CLASSIFICATION FOR SUPPLY</b>
--

<b>15. INSTRUCTIONS ON USE</b>
--------------------------------

<b>16. INFORMATION IN BRAILLE</b>
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Tremfya 100 mg

<b>17. UNIQUE IDENTIFIER – 2D BARCODE</b>
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<b>18. UNIQUE IDENTIFIER - HUMAN READABLE DATA</b>
--

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING****CARTON FOR PRE-FILLED PEN MULTIPACK COMPRISING 2 PACKS (INCLUDING BLUE BOX)****1. NAME OF THE MEDICINAL PRODUCT**

Tremfya 100 mg solution for injection in pre-filled pen  
guselkumab

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each pre-filled pen contains 100 mg of guselkumab in 1 mL.

**3. LIST OF EXCIPIENTS**

Excipients: sucrose, histidine, histidine monohydrochloride monohydrate, polysorbate 80, water for injections.

**4. PHARMACEUTICAL FORM AND CONTENTS**

Solution for injection

Multipack: 2 (2 packs of 1) pre-filled pens

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Do not shake  
Subcutaneous use  
Read the package leaflet before use.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY****8. EXPIRY DATE**

EXP

**9. SPECIAL STORAGE CONDITIONS**

Store in a refrigerator.

Do not freeze.

Keep the pre-filled pen in the outer carton in order to protect from light.

<b>10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE</b>
--

<b>11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER</b>
---

Janssen-Cilag International NV  
Turnhoutseweg 30  
B-2340 Beerse  
Belgium

<b>12. MARKETING AUTHORISATION NUMBER(S)</b>
--

EU/1/17/1234/003 (2 packs, each containing 1 pre-filled pen)

<b>13. BATCH NUMBER</b>
-------------------------

Lot

<b>14. GENERAL CLASSIFICATION FOR SUPPLY</b>
--

<b>15. INSTRUCTIONS ON USE</b>
--------------------------------

<b>16. INFORMATION IN BRAILLE</b>
-----------------------------------

Tremfya 100 mg

<b>17. UNIQUE IDENTIFIER – 2D BARCODE</b>
---

2D barcode carrying the unique identifier included.

<b>18. UNIQUE IDENTIFIER - HUMAN READABLE DATA</b>
--

PC  
SN  
NN

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**PRE-FILLED PEN LABEL TEXT (100 mg)**

**1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION**

Tremfya 100 mg  
injection  
guselkumab  
SC

**2. METHOD OF ADMINISTRATION**

**3. EXPIRY DATE**

EXP

**4. BATCH NUMBER**

Lot

**5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT**

1 mL

**6. OTHER**

## **B. PACKAGE LEAFLET**

## **Package leaflet: Information for the user**

### **Tremfya 100 mg solution for injection in pre-filled syringe** guselkumab

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

#### **Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

#### **What is in this leaflet**

1. What Tremfya is and what it is used for
2. What you need to know before you use Tremfya
3. How to use Tremfya
4. Possible side effects
5. How to store Tremfya
6. Contents of the pack and other information

#### **1. What Tremfya is and what it is used for**

Tremfya contains the active substance guselkumab which is a type of protein called a monoclonal antibody.

This medicine works by blocking the activity of a protein called IL-23, which is present at increased levels in people with psoriasis and psoriatic arthritis.

##### **Plaque psoriasis**

Tremfya is used to treat adults with moderate to severe “plaque psoriasis”, an inflammatory condition affecting the skin and nails.

Tremfya can improve the condition of the skin and appearance of nails and reduce symptoms, such as scaling, shedding, flaking, itching, pain and burning.

##### **Psoriatic arthritis**

Tremfya is used to treat a condition called “psoriatic arthritis”, an inflammatory disease of the joints, often accompanied by psoriasis. If you have psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Tremfya to reduce the signs and symptoms of the disease. Tremfya can be used alone or with another medicine named methotrexate.

Using Tremfya in psoriatic arthritis will benefit you by reducing the signs and symptoms of the disease, slowing down the damage to the cartilage and bone of the joints and improving your ability to do normal daily activities.



## **2. What you need to know before you use Tremfya**

### **Do not use Tremfya**

- if you are allergic to guselkumab or any of the other ingredients of this medicine (listed in section 6). If you think you may be allergic, ask your doctor for advice before using Tremfya
- if you have an active infection, including active tuberculosis

### **Warnings and precautions**

Talk to your doctor, pharmacist or nurse before using Tremfya:

- if you are being treated for an infection
- if you have an infection that does not go away or that keeps coming back
- if you have tuberculosis or have been in close contact with someone with tuberculosis
- if you think you have an infection or have symptoms of an infection (see below under ‘Look out for infections and allergic reactions’)
- if you have recently had a vaccination or if you are due to have a vaccination during treatment with Tremfya.

If you are not sure if any of the above applies to you, talk to your doctor, pharmacist or nurse before using Tremfya.

As directed by your doctor, you may need blood tests to check if you have high levels of liver enzymes before you start taking Tremfya and when using it. Increases in liver enzymes may occur more frequently in patients receiving Tremfya every 4 weeks than in patients receiving Tremfya every 8 weeks (see “How to use Tremfya” in section 3).

### **Look out for infections and allergic reactions**

Tremfya can potentially cause serious side effects, including allergic reactions and infections. You must look out for signs of these conditions while you are taking Tremfya. Stop using Tremfya and tell your doctor or seek medical help immediately if you notice any signs indicating a possible serious allergic reaction or an infection.

Signs of infections may include fever or flu like symptoms; muscle aches; cough; shortness of breath; burning when you urinate or urinating more often than usual; blood in your phlegm (mucus); weight loss; diarrhoea or stomach pain; warm, red, or painful skin or sores on your body which are different from your psoriasis.

Serious allergic reactions, which can include the following symptoms, swollen face, lips, mouth, tongue or throat, difficulty swallowing or breathing and hives, have occurred with Tremfya (see “Serious side effects” in section 4).

### **Children and adolescents**

Tremfya is not recommended for children and adolescents under 18 years of age because it has not been studied in this age group.

### **Other medicines and Tremfya**

Tell your doctor or pharmacist:

- if you are using, have recently used or might use any other medicines.
- if you recently had or are due to have a vaccination. You should not be given certain types of vaccines (live vaccines) while using Tremfya.

### **Pregnancy and breast-feeding**

- Tremfya should not be used in pregnancy as the effects of this medicine in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and must use adequate contraception while using Tremfya and for at least 12 weeks after the last Tremfya dose. Talk to your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.

- Talk to your doctor if you are breast-feeding or are planning to breast-feed. You and your doctor should decide if you will breast-feed or use Tremfya.

### **Driving and using machines**

Tremfya is unlikely to influence your ability to drive and use machines.

## **3. How to use Tremfya**

Always use this medicine exactly as your doctor or nurse has told you. Check with your doctor, nurse or pharmacist if you are not sure.

### **How much Tremfya is given and for how long**

Your doctor will decide for how long you need to use Tremfya.

#### Plaque psoriasis

- The dose is 100 mg (the content of 1 pre-filled syringe) given by injection under the skin (subcutaneous injection). This may be given by your doctor or nurse.
- After the first dose, you will have the next dose 4 weeks later, and then every 8 weeks.

#### Psoriatic arthritis

- The dose is 100 mg (the content of 1 pre-filled syringe) given by injection under the skin (subcutaneous injection). This may be given by your doctor or nurse.
- After the first dose, you will receive the next dose 4 weeks later, and then every 8 weeks. For some patients, after the first dose, Tremfya may be given every 4 weeks. Your doctor will decide how often you may receive Tremfya.

At the start, your doctor or nurse will inject Tremfya. However, you may decide together with your doctor to give Tremfya yourself in which case you will get the appropriate training on how to inject Tremfya. Talk to your doctor or nurse if you have any questions about giving yourself an injection. It is important not to try to inject yourself until you have been trained by your doctor or nurse.

For detailed instructions on how to use Tremfya, carefully read the 'Instructions for use' leaflet before use, which is included in the carton.

### **If you use more Tremfya than you should**

If you have received more Tremfya than you should or the dose has been given sooner than prescribed, inform your doctor.

### **If you forget to use Tremfya**

If you have forgotten to inject a dose of Tremfya, inform your doctor.

### **If you stop using Tremfya**

You should not stop using Tremfya without speaking to your doctor first. If you stop treatment, your symptoms may come back.

## **4. Possible side effects**

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

### **Serious side effects**

Tell your doctor or seek medical help immediately if you get any of the following side effects:

**Possible serious allergic reaction** (may affect up to 1 in 100 people) - the signs may include:

- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat

- severe itching of the skin, with a red rash or raised bumps

### **Other side effects**

The following side effects are all mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse immediately.

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

- respiratory tract infections

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

- headache
- joint pain (arthralgia)
- diarrhoea
- redness, irritation or pain at the injection site
- increased level of liver enzymes in the blood

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

- allergic reaction
- skin rash
- decreased number of a type of white blood cell called neutrophils
- herpes simplex infections
- fungal infection of the skin, for instance between the toes (e.g., athlete's foot)
- stomach flu (gastroenteritis)
- hives

### **Reporting of side effects**

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via **the national reporting system** listed in [Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

## **5. How to store Tremfya**

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the syringe label and on the outer carton after "EXP". The expiry date refers to the last day of that month.

Keep the pre-filled syringe in the outer carton in order to protect it from light.

Store in a refrigerator (2°C–8°C). Do not freeze.

Do not shake.

Do not use this medicine if you notice that the medicine is cloudy or discoloured, or contains large particles. Before use, remove the carton from the refrigerator and keep the pre-filled syringe inside the carton and allow to reach room temperature by waiting for 30 minutes.

This medicine is for single use only. Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

## **6. Contents of the pack and other information**

### **What Tremfya contains**

- The active substance is guselkumab. Each pre-filled syringe contains 100 mg of guselkumab in 1 mL solution.
- The other ingredients are histidine, histidine monohydrochloride monohydrate, polysorbate 80, sucrose and water for injections.

### **What Tremfya looks like and contents of the pack**

Solution for injection (injection). Tremfya is a clear, colourless to light yellow solution. It is supplied as a carton pack containing one single-dose glass syringe and as a multipack containing 2 (2 packs of 1) single-dose pre-filled syringes. Not all pack sizes may be marketed.

### **Marketing Authorisation Holder**

Janssen-Cilag International NV  
Turnhoutseweg 30  
B-2340 Beerse  
Belgium

### **Manufacturer**

Janssen Biologics B.V.  
Einsteinweg 101  
2333CB Leiden  
The Netherlands

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

#### **België/Belgique/Belgien**

Janssen-Cilag NV  
Antwerpseweg 15-17  
B-2340 Beerse  
Tel/Tél: +32 14 64 94 11

#### **Lietuva**

UAB "JOHNSON & JOHNSON"  
Konstitucijos pr. 21C  
LT-08130 Vilnius  
Tel: +370 5 278 68 88

#### **България**

„Джонсън & Джонсън България“ ЕООД  
ж.к. Младост 4  
Бизнес Парк София, сграда 4  
София 1766  
Тел.: +359 2 489 94 00

#### **Luxembourg/Luxemburg**

Janssen-Cilag NV  
Antwerpseweg 15-17  
B-2340 Beerse  
Belgique/Belgien  
Tél/Tel: +32 14 64 94 11

#### **Česká republika**

Janssen-Cilag s.r.o.  
Walterovo náměstí 329/1  
CZ-158 00 Praha 5 – Jinonice  
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#### **Magyarország**

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**This leaflet was last revised in**

Detailed information on this medicine is available on the European Medicines Agency web site:  
<http://www.ema.europa.eu>.

## Instructions for use

### Tremfya

#### Pre-filled syringe



SINGLE-USE

### Important

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

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 doctor about your medical condition or your treatment. Please also read the Package Leaflet carefully before starting your injection and discuss any questions you may have with your doctor or nurse.

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



### Storage information

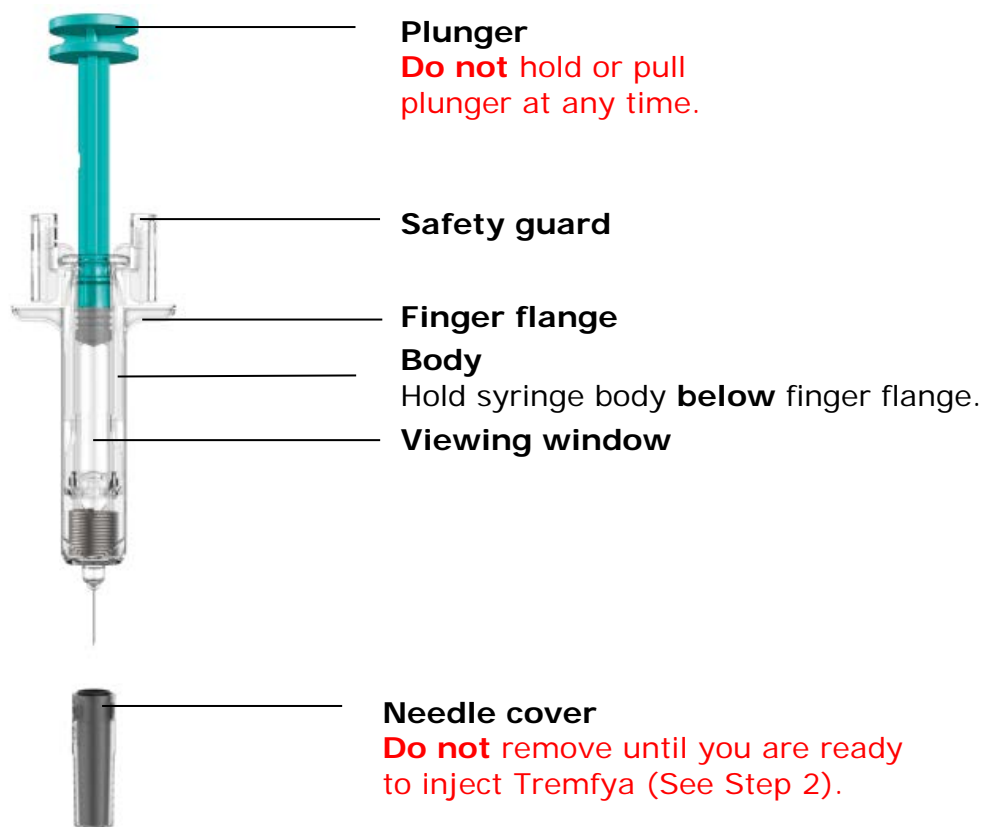
Store in refrigerator at 2° to 8°C. **Do not** freeze.

**Keep Tremfya and all medicines out of reach of children.**

**Do not** shake the pre-filled syringe at any time.

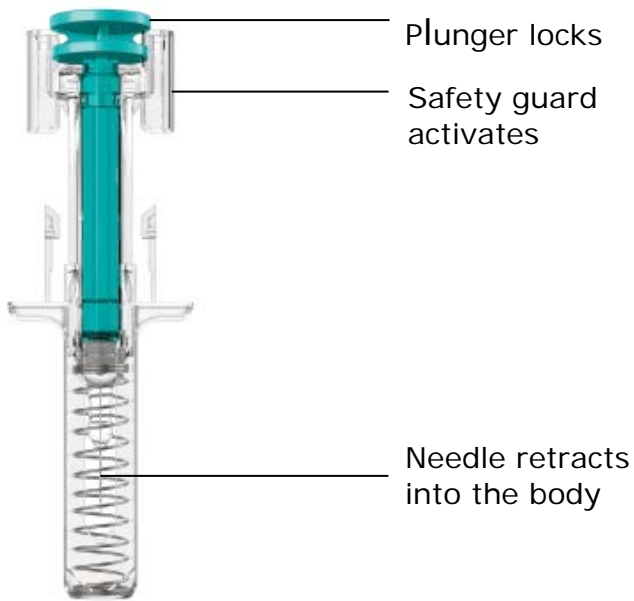
## Pre-filled syringe at-a-glance

Before injection





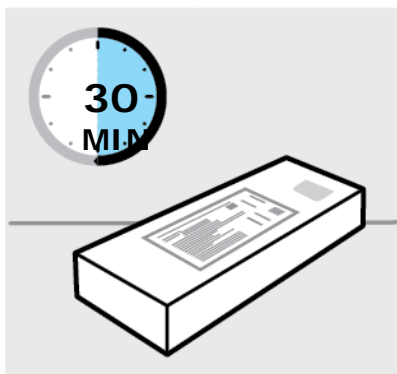
After injection



**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

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 if the perforations on the carton are broken.

Call your doctor or pharmacist for a refill.



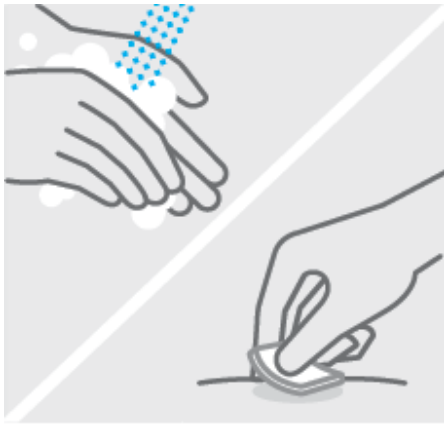
### Choose injection site

Select from the following areas for your injection:

- **Front of thighs** (recommended)
- Lower abdomen
  - Do not** use the 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 or hard.

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

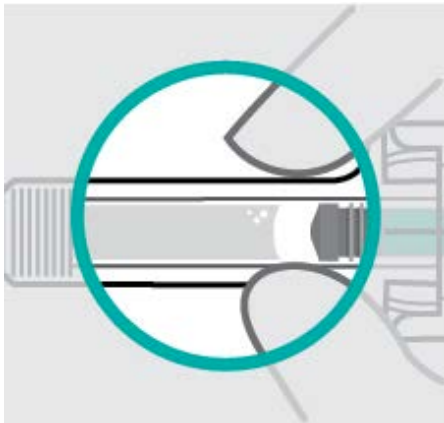


## Clean injection site

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

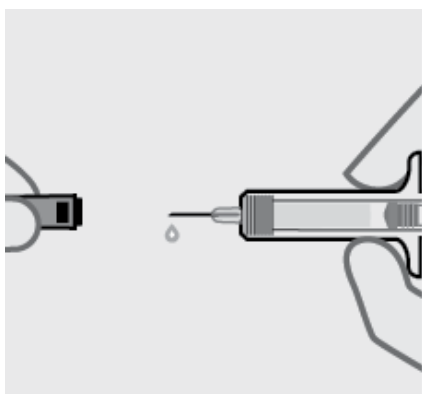
Take the pre-filled syringe out of the carton.

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 discoloured, or has large particles. If you are uncertain, call your doctor or pharmacist for a refill.

## 2. Inject Tremfya using the pre-filled syringe



### Remove needle cover

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

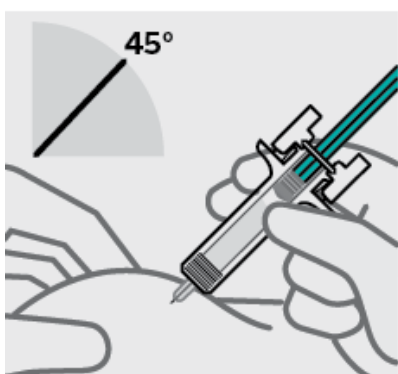
It is normal to see a drop of liquid.

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

**Do not** put needle cover back on, as this may damage the needle.

**Do not** touch needle or let it touch any surface.

**Do not** use the Tremfya pre-filled syringe if it is dropped. Call your doctor or pharmacist for a refill.



### Position fingers and insert needle

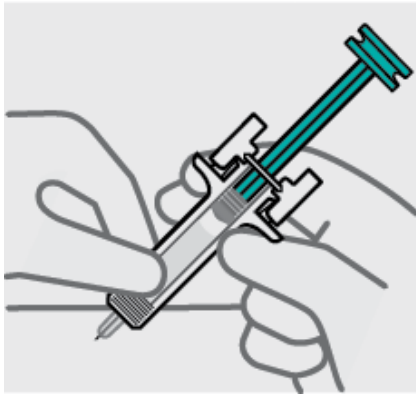
Place your thumb, index and middle fingers **directly under the finger flange**, as shown.

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

Use your other hand to pinch skin at the injection site. Position syringe at about a 45 degree angle to the skin.

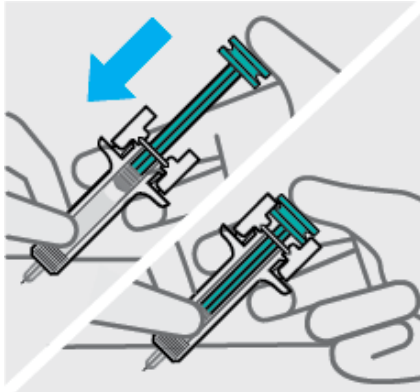
It is important to pinch enough skin to **inject under the skin** and not into the muscle.

Insert needle with a quick, dart-like motion.



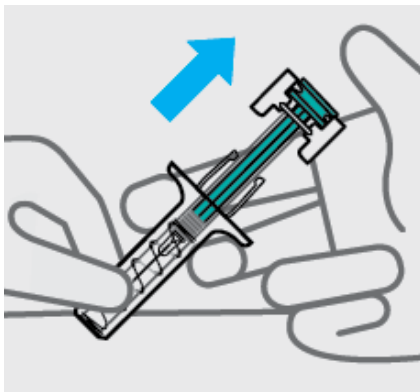
### **Release pinch and reposition hand**

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



### **Press plunger**

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



### **Release pressure from plunger**

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

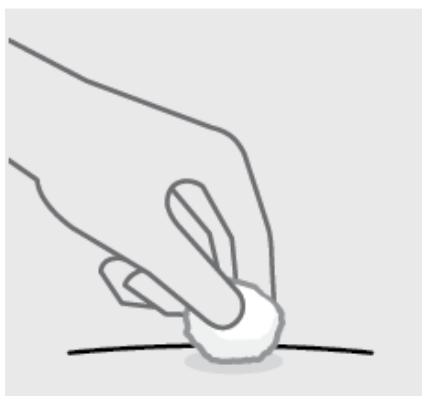
### 3. After your injection



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

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

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



#### Check injection site

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

**Do not** rub the injection site.

If needed, cover injection site with a bandage.

Your injection is now complete!



#### Need help?

Call your doctor to talk about any questions you may have. For additional assistance or to share your feedback refer to the Package Leaflet for your local representative contact information.

## **Package leaflet: Information for the user**

### **Tremfya 100 mg solution for injection in pre-filled pen** guselkumab

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

#### **What is in this leaflet**

1. What Tremfya is and what it is used for
2. What you need to know before you use Tremfya
3. How to use Tremfya
4. Possible side effects
5. How to store Tremfya
6. Contents of the pack and other information

#### **1. What Tremfya is and what it is used for**

Tremfya contains the active substance guselkumab which is a type of protein called a monoclonal antibody.

This medicine works by blocking the activity of a protein called IL-23, which is present at increased levels in people with psoriasis and psoriatic arthritis.

##### **Plaque Psoriasis**

Tremfya is used to treat adults with moderate to severe “plaque psoriasis”, an inflammatory condition affecting the skin and nails.

Tremfya can improve the condition of the skin and appearance of nails and reduce symptoms, such as scaling, shedding, flaking, itching, pain and burning.

##### **Psoriatic arthritis**

Tremfya is used to treat a condition called “psoriatic arthritis”, an inflammatory disease of the joints, often accompanied by psoriasis. If you have psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Tremfya to reduce the signs and symptoms of the disease. Tremfya can be used alone or with another medicine named methotrexate.

Using Tremfya in psoriatic arthritis will benefit you by reducing the signs and symptoms of the disease, slowing down the damage to the cartilage and bone of the joints and improving your ability to do normal daily activities.

## **2. What you need to know before you use Tremfya**

### **Do not use Tremfya**

- if you are allergic to guselkumab or any of the other ingredients of this medicine (listed in section 6). If you think you may be allergic, ask your doctor for advice before using Tremfya
- if you have an active infection, including active tuberculosis

### **Warnings and precautions**

Talk to your doctor, pharmacist or nurse before using Tremfya:

- if you are being treated for an infection
- if you have an infection that does not go away or that keeps coming back
- if you have tuberculosis or have been in close contact with someone with tuberculosis
- if you think you have an infection or have symptoms of an infection (see below under ‘Look out for infections and allergic reactions’)
- if you have recently had a vaccination or if you are due to have a vaccination during treatment with Tremfya.

If you are not sure if any of the above applies to you, talk to your doctor, pharmacist or nurse before using Tremfya.

As directed by your doctor, you may need blood tests to check if you have high levels of liver enzymes before you start taking Tremfya and when using it. Increases in liver enzymes may occur more frequently in patients receiving Tremfya every 4 weeks than in patients receiving Tremfya every 8 weeks (see “How to use Tremfya” in section 3).

### **Look out for infections and allergic reactions**

Tremfya can potentially cause serious side effects, including allergic reactions and infections. You must look out for signs of these conditions while you are taking Tremfya. Stop using Tremfya and tell your doctor or seek medical help immediately if you notice any signs indicating a possible serious allergic reaction or an infection.

Signs of infections may include fever or flu like symptoms; muscle aches; cough; shortness of breath; burning when you urinate or urinating more often than usual; blood in your phlegm (mucus); weight loss; diarrhoea or stomach pain; warm, red, or painful skin or sores on your body which are different from your psoriasis.

Serious allergic reactions, which can include the following symptoms, swollen face, lips, mouth, tongue or throat, difficulty swallowing or breathing and hives, have occurred with Tremfya (see “Serious side effects” in section 4).

### **Children and adolescents**

Tremfya is not recommended for children and adolescents under 18 years of age because it has not been studied in this age group.

### **Other medicines and Tremfya**

Tell your doctor or pharmacist:

- if you are using, have recently used or might use any other medicines.
- if you recently had or are due to have a vaccination. You should not be given certain types of vaccines (live vaccines) while using Tremfya.

### **Pregnancy and breast-feeding**

- Tremfya should not be used in pregnancy as the effects of this medicine in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and must use adequate contraception while using Tremfya and for at least 12 weeks



after the last Tremfya dose. Talk to your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.

- Talk to your doctor if you are breast-feeding or are planning to breast-feed. You and your doctor should decide if you will breast-feed or use Tremfya.

### **Driving and using machines**

Tremfya is unlikely to influence your ability to drive and use machines.

## **3. How to use Tremfya**

Always use this medicine exactly as your doctor or nurse has told you. Check with your doctor, nurse or pharmacist if you are not sure.

### **How much Tremfya is given and for how long**

Your doctor will decide for how long you need to use Tremfya.

#### Plaque psoriasis

- The dose is 100 mg (the content of 1 pre-filled pen) given by injection under the skin (subcutaneous injection). This may be given by your doctor or nurse.
- After the first dose, you will have the next dose 4 weeks later, and then every 8 weeks.

#### Psoriatic arthritis

- The dose is 100 mg (the content of 1 pre-filled pen) given by injection under the skin (subcutaneous injection). This may be given by your doctor or nurse.
- After the first dose, you will receive the next dose 4 weeks later, and then every 8 weeks. For some patients, after the first dose, Tremfya may be given every 4 weeks. Your doctor will decide how often you may receive Tremfya.

At the start, your doctor or nurse will inject Tremfya. However, you may decide together with your doctor to give Tremfya yourself in which case you will get the appropriate training on how to inject Tremfya. Talk to your doctor or nurse if you have any questions about giving yourself an injection. It is important not to try to inject yourself until you have been trained by your doctor or nurse.

For detailed instructions on how to use Tremfya, carefully read the 'Instructions for use' leaflet before use, which is included in the carton.

### **If you use more Tremfya than you should**

If you have received more Tremfya than you should or the dose has been given sooner than prescribed, inform your doctor.

### **If you forget to use Tremfya**

If you have forgotten to inject a dose of Tremfya, inform your doctor.

### **If you stop using Tremfya**

You should not stop using Tremfya without speaking to your doctor first. If you stop treatment, your symptoms may come back.

## **4. Possible side effects**

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

### **Serious side effects**

Tell your doctor or seek medical help immediately if you get any of the following side effects:

**Possible serious allergic reaction** (may affect up to 1 in 100 people) - the signs may include:

- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps

### **Other side effects**

The following side effects are all mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse immediately.

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

- respiratory tract infections

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

- headache
- joint pain (arthralgia)
- diarrhoea
- redness, irritation or at the injection site
- increased level of liver enzymes in the blood

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

- allergic reaction
- skin rash
- decreased number of a type of white blood cell called neutrophils
- herpes simplex infections
- fungal infection of the skin, for instance between the toes (e.g., athlete's foot)
- stomach flu (gastroenteritis)
- hives

### **Reporting of side effects**

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [the national reporting system listed in Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

## **5. How to store Tremfya**

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the pre-filled pen label and on the outer carton after "EXP". The expiry date refers to the last day of that month.

Keep the pre-filled pen in the outer carton in order to protect it from light.

Store in a refrigerator (2°C–8°C). Do not freeze.

Do not shake.

Do not use this medicine if you notice that the medicine is cloudy or discoloured, or contains large particles. Before use, remove the carton from the refrigerator and keep the pre-filled pen inside the carton and allow to reach room temperature by waiting for 30 minutes.

This medicine is for single use only. Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

## **6. Contents of the pack and other information**

### **What Tremfya contains**

- The active substance is guselkumab. Each pre-filled pen contains 100 mg of guselkumab in 1 mL solution.
- The other ingredients are histidine, histidine monohydrochloride monohydrate, polysorbate 80, sucrose and water for injections.

### **What Tremfya looks like and contents of the pack**

Solution for injection (injection). Tremfya is a clear, colourless to light yellow solution. It is supplied as a carton pack containing one single-dose pre-filled pen and as a multipack containing 2 (2 packs of 1) single-dose pre-filled pens. Not all pack sizes may be marketed.

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### **Manufacturer**

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Detailed information on this medicine is available on the European Medicines Agency web site:  
<http://www.ema.europa.eu>.

## Instructions for use

### Tremfya

#### Pre-filled pen



SINGLE-USE DEVICE

### Important

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

Please read these Instructions for use before using the Tremfya pre-filled pen and each time you get a new pre-filled pen. There may be new information. This instruction guide does not take the place of talking with your doctor about your medical condition or your treatment.

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



### Storage information

Store in refrigerator at 2° to 8°C.

**Do not** freeze.

**Keep Tremfya and all medicines out of reach of children.**

**Do not** shake your pre-filled pen at any time.



### Need help?

Call your doctor to talk about any questions you may have. For additional assistance or to share your feedback refer to the Package Leaflet for your local representative contact information.

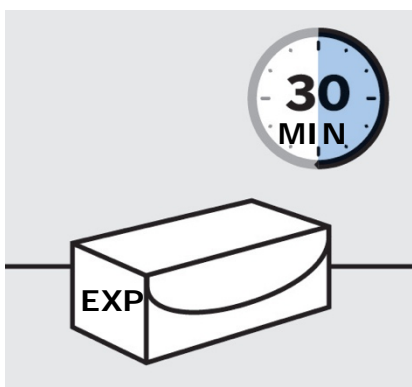
## Pre-filled pen at-a-glance



### 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

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

Keep pre-filled pen 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 carton.

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

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

Call your doctor or pharmacist for a new pre-filled pen.



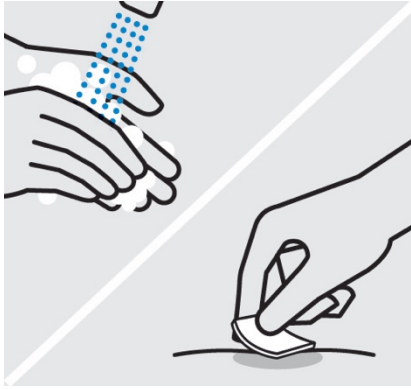
### Choose injection site

Select from the following areas for your injection:

- **Front of thighs** (recommended)
- Lower abdomen  
**Do not** use the 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**

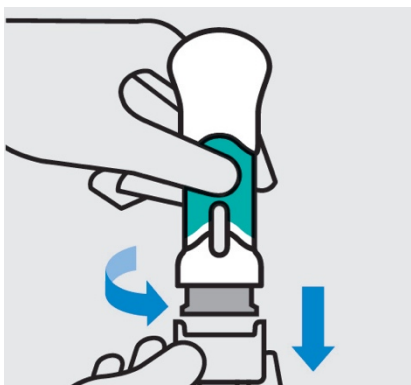
Take the pre-filled pen out of the carton.

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

This is normal.

**Do not** inject if the liquid is cloudy or discoloured, or has large particles. If you are uncertain, call your doctor or pharmacist for a new pre-filled pen.

## 2. Inject Tremfya using the pre-filled pen



### **Twist and pull off bottom cap**

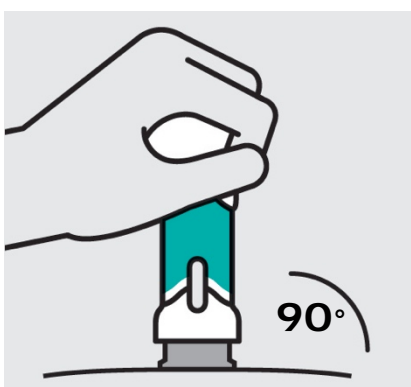
Keep hands away from the needle guard after the cap is removed.

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

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

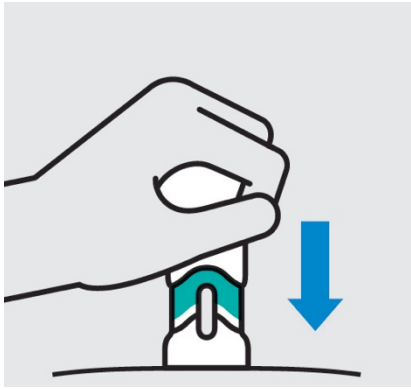
**Do not** use the pre-filled pen if it is dropped after removing the cap.

Call your doctor or pharmacist for a new pre-filled pen.



### **Place on skin**

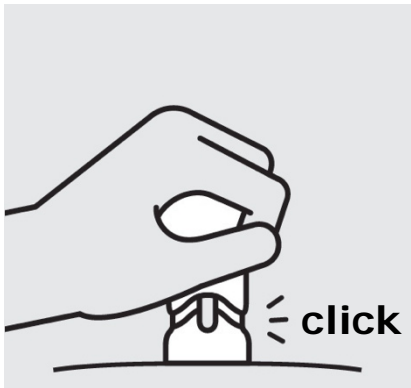
Position the pre-filled pen straight onto the skin (about 90 degrees relative to injection site).



### **Push handle straight down**

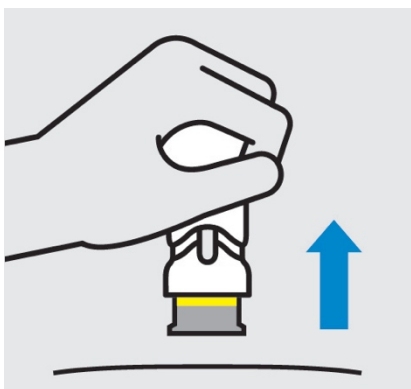
Medication injects as you push. Do this at a speed that is comfortable for you.

**Do not** lift the pre-filled pen during the injection. The needle guard will lock and the full dose will not be delivered.



### **Complete injection**

Injection is complete when the handle is pushed all the way down, you hear a click, and the green body is no longer visible.



### **Lift straight up**

The yellow band indicates that the needle guard is locked.

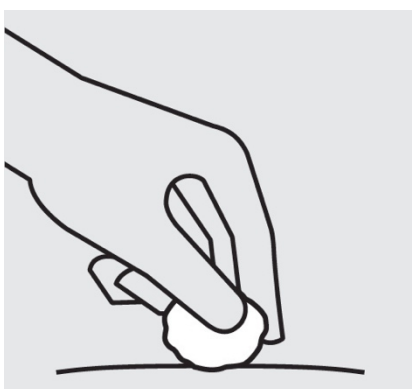
### 3. After your injection



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

Put your used pre-filled pen in a sharps disposal container right away after use.

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



#### **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.

Your injection is now complete!