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.

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

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

Guselkumab is a fully human immunoglobulin G1 lambda (IgG1λ) 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**

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

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 plaque psoriasis.

**Posology**

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.

*Elderly (≥ 65 years)*

No dose adjustment is required (see section 5.2).

There is limited information in subjects aged ≥ 65 years.

*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 yet
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**

If a serious hypersensitivity reaction occurs, administration of Tremfya should be discontinued immediately and appropriate therapy initiated.

**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
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. Because immunoglobulins are excreted in human milk, a risk to the breast-feeding child cannot be excluded. A decision should be made whether to discontinue breast-feeding during treatment and up to 12 weeks after the last dose, or to discontinue 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
A total of 1748 patients were treated with Tremfya in one phase II and three phase III studies in plaque psoriasis. Of these, 1393 psoriasis subjects were exposed to Tremfya for at least 6 months and 728 subjects were exposed for at least 1 year (i.e., treated through week 48).

The frequencies of the specified adverse reactions were determined from the pooled analysis of 823 patients with moderate to severe plaque psoriasis receiving Tremfya during the placebo-controlled periods of two phase III studies.
The adverse reactions (Table 1) are classified by MedDRA System Organ Class and frequency, using the following convention: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000), not known (cannot be estimated from the available data).

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Frequency</th>
<th>ADR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections and infestations</td>
<td>Very common</td>
<td>Upper respiratory infection</td>
</tr>
<tr>
<td></td>
<td>Common</td>
<td>Gastroenteritis</td>
</tr>
<tr>
<td></td>
<td>Common</td>
<td>Herpes simplex infections</td>
</tr>
<tr>
<td></td>
<td>Common</td>
<td>Tinea infections</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Common</td>
<td>Headache</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Common</td>
<td>Diarrhoea</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Common</td>
<td>Urticaria</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>Common</td>
<td>Arthralgia</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Common</td>
<td>Injection site erythema</td>
</tr>
<tr>
<td></td>
<td>Uncommon</td>
<td>Injection site pain</td>
</tr>
</tbody>
</table>

Description of selected adverse reactions

**Gastroenteritis**

In two phase III 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%). Adverse reactions of gastroenteritis were non-serious and did not lead to discontinuation of Tremfya through Week 48.

**Injection site reactions**

In two phase III clinical studies through Week 48, 0.7% of Tremfya injections and 0.3% of placebo injections were associated with injection site reactions. Adverse reactions of injection site erythema and injection site pain were all mild to moderate in severity, none were serious, and none led to discontinuation of Tremfya.

**Immunogenicity**

The immunogenicity of Tremfya was evaluated using a sensitive and drug-tolerant immunoassay. In pooled phase II and phase III analyses, fewer than 6% of subjects treated with Tremfya developed antidrug antibodies in up to 52 weeks of treatment. Of the subjects who developed antidrug antibodies, approximately 7% had antibodies that were classified as neutralizing, which equates to 0.4% of all subjects treated with Tremfya. Antidrug antibodies were not associated with lower efficacy or development of injection-site reactions.

**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 overdosage, 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: not yet assigned.

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 Te17 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 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 studies. These results are consistent with the clinical benefit observed with guselkumab treatment in plaque psoriasis.

Clinical efficacy and safety
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 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). PASI 90 non-responders from the adalimumab group started to receive guselkumab at Weeks 28 and 32 and q8w thereafter. All patients were followed for up to 48 weeks following first administration of study treatment.

Baseline disease characteristics were consistent for the study populations in VOYAGE 1 and 2 with a median BSA of 22% and 24%, a median baseline PASI score of 19 for both studies, a median baseline DLQI score of 14 and 14.5, a baseline 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 (TNFα) 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 2).

**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 2 below.

<table>
<thead>
<tr>
<th>Table 2: Summary of Clinical Responses in VOYAGE 1 and VOYAGE 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Number of patients (%)</strong></td>
</tr>
<tr>
<td><strong>Week 16</strong></td>
</tr>
<tr>
<td>Placebo (N=174)</td>
</tr>
<tr>
<td>Vaselkumab (N=329)</td>
</tr>
<tr>
<td>Adalimumab (N=334)</td>
</tr>
<tr>
<td>Placebo (N=248)</td>
</tr>
<tr>
<td>Vaselkumab (N=496)</td>
</tr>
<tr>
<td>Adalimumab (N=248)</td>
</tr>
<tr>
<td>PASI 75</td>
</tr>
<tr>
<td>10 (5.7)</td>
</tr>
<tr>
<td>300 (91.2)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>244 (73.1)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>20 (8.1)</td>
</tr>
<tr>
<td>428 (86.3)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>170 (68.5)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>PASI 90</td>
</tr>
<tr>
<td>5 (2.9)</td>
</tr>
<tr>
<td>241 (73.3)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>166 (49.7)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>6 (2.4)</td>
</tr>
<tr>
<td>347 (70.0)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>116 (46.8)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>PASI 100</td>
</tr>
<tr>
<td>1 (0.6)</td>
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<tr>
<td>123 (37.4)&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>57 (17.1)&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>2 (0.8)</td>
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<tr>
<td>169 (34.1)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>51 (20.6)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>IGA 0/1</td>
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<tr>
<td>12 (6.9)</td>
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<tr>
<td>280 (85.1)&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>220 (65.9)&lt;sup&gt;b&lt;/sup&gt;</td>
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<tr>
<td>21 (8.5)</td>
</tr>
<tr>
<td>417 (84.1)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>168 (67.7)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>IGA 0</td>
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<tr>
<td>2 (1.1)</td>
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<tr>
<td>157 (47.7)&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>88 (26.3)&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>2 (0.8)</td>
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<tr>
<td>215 (43.3)&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>71 (28.6)&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td><strong>Week 24</strong></td>
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<tr>
<td>Placebo (N=174)</td>
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<tr>
<td>Vaselkumab (N=329)</td>
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<td>Adalimumab (N=334)</td>
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<tr>
<td>Placebo (N=248)</td>
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<td>PASI 75</td>
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<td>-</td>
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<tr>
<td>300 (91.2)&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>241 (72.2)&lt;sup&gt;c&lt;/sup&gt;</td>
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<td>-</td>
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<td>442 (89.1)</td>
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<td>176 (71.0)&lt;sup&gt;c&lt;/sup&gt;</td>
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<td>PASI 90</td>
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<td>-</td>
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<td>264 (80.2)</td>
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<tr>
<td>177 (53.0)&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>-</td>
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<tr>
<td>373 (75.2)</td>
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<tr>
<td>136 (54.8)&lt;sup&gt;b&lt;/sup&gt;</td>
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<tr>
<td>PASI 100</td>
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<td>-</td>
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<tr>
<td>146 (44.4)</td>
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<td>83 (24.9)&lt;sup&gt;c&lt;/sup&gt;</td>
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<td>219 (44.2)</td>
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<td>66 (26.6)&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>IGA 0/1</td>
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<tr>
<td>277 (84.2)</td>
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<td>206 (61.7)&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>-</td>
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<tr>
<td>414 (83.5)</td>
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<td>161 (64.9)&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>IGA 0</td>
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<td>-</td>
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<td>173 (52.6)</td>
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<tr>
<td>98 (29.3)&lt;sup&gt;c&lt;/sup&gt;</td>
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<td>-</td>
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<td>257 (51.8)</td>
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<tr>
<td>78 (31.5)&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td><strong>Week 48</strong></td>
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<tr>
<td>Placebo (N=174)</td>
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<tr>
<td>Vaselkumab (N=329)</td>
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<td>PASI 90</td>
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<td>251 (76.3)</td>
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<td>PASI 100</td>
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<td>156 (47.4)</td>
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<td>166 (50.5)</td>
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</tbody>
</table>

<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 subjects 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).
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-naive, biologic-naive, 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.

In VOYAGE 2, among 112 adalimumab subjects who failed to achieve a PASI 90 response at Week 28, 66% achieved a PASI 90 response after 20 weeks of treatment with guselkumab. 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 3). 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 ≤ 0.001, except for hand and foot psoriasis at Week 24 [VOYAGE 2] and Week 48 [VOYAGE 1], p < 0.05).

Figure 1: Percent of Subjects Who Achieved PASI 90 Response Through Week 48 by Visit (Subjects Randomised at Week 0) in VOYAGE 1
Table 3: Summary of Regional Disease Responses in VOYAGE 1 and VOYAGE 2

<table>
<thead>
<tr>
<th>Placebo</th>
<th>VOYAGE 1</th>
<th>Adalimumab</th>
<th>Placebo</th>
<th>VOYAGE 2</th>
<th>Adalimumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>ss-IGA (N)</td>
<td>145</td>
<td>277</td>
<td>286</td>
<td>202</td>
<td>408</td>
</tr>
<tr>
<td>ss-IGA 0/1, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 16</td>
<td>21 (14.5)</td>
<td>231 (83.4)c</td>
<td>201 (70.3)d</td>
<td>22 (10.9)</td>
<td>329 (80.6)c</td>
</tr>
<tr>
<td>hf-PGA (N)</td>
<td>43</td>
<td>90</td>
<td>95</td>
<td>63</td>
<td>114</td>
</tr>
<tr>
<td>hf-PGA 0/1, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 16</td>
<td>6 (14.0)</td>
<td>66 (73.3)c</td>
<td>53 (55.8)d</td>
<td>9 (14.3)</td>
<td>88 (77.2)c</td>
</tr>
<tr>
<td>f-PGA (N)</td>
<td>88</td>
<td>174</td>
<td>173</td>
<td>123</td>
<td>246</td>
</tr>
<tr>
<td>f-PGA 0/1, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 16</td>
<td>14 (15.9)</td>
<td>68 (39.1)c</td>
<td>80 (50.9)d</td>
<td>18 (14.6)</td>
<td>128 (52.0)c</td>
</tr>
<tr>
<td>NAPSI (N)</td>
<td>99</td>
<td>194</td>
<td>191</td>
<td>140</td>
<td>280</td>
</tr>
<tr>
<td>Percent Improvement, mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 16</td>
<td>-0.9 (57.9)</td>
<td>34.4 (42.4)c</td>
<td>38.0 (53.9)d</td>
<td>1.8 (53.8)</td>
<td>39.6 (45.6)c</td>
</tr>
</tbody>
</table>

a Includes only subjects with ss-IGA, f-PGA, hf-PGA score ≥ 2 at baseline or baseline NAPSI score > 0.
b Includes only subjects achieving ≥ 2-grade improvement from baseline in ss-IGA and/or hf-PGA.
c p < 0.001 for comparison between guselkumab and placebo for the major secondary endpoint.
d comparisons between guselkumab and adalimumab were not performed.
e 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 4). Signs of improvement on patient-reported outcomes were maintained through Week 24 (VOYAGE 1 and 2) and Week 48 (VOYAGE 1).

Table 4: Summary of Patient Reported Outcomes in VOYAGE 1 and VOYAGE 2

<table>
<thead>
<tr>
<th>Placebo</th>
<th>VOYAGE 1</th>
<th>Adalimumab</th>
<th>Placebo</th>
<th>VOYAGE 2</th>
<th>Adalimumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLQI, subjects with baseline score</td>
<td>170</td>
<td>322</td>
<td>328</td>
<td>248</td>
<td>495</td>
</tr>
<tr>
<td>Change from baseline, mean (standard deviation)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 16</td>
<td>-0.6 (6.4)</td>
<td>-11.2 (7.2)c</td>
<td>-9.3 (7.8)d</td>
<td>-2.6 (6.9)</td>
<td>-11.3 (6.8)c</td>
</tr>
<tr>
<td>PSSD Symptom score, subjects with baseline score &gt; 0</td>
<td>129</td>
<td>248</td>
<td>273</td>
<td>198</td>
<td>410</td>
</tr>
<tr>
<td>Symptom score = 0, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 16</td>
<td>1 (0.8)</td>
<td>67 (27.0)c</td>
<td>45 (16.5)b</td>
<td>0</td>
<td>112 (27.3)c</td>
</tr>
<tr>
<td>PSSD Sign score, subjects with baseline score &gt; 0</td>
<td>129</td>
<td>248</td>
<td>274</td>
<td>198</td>
<td>411</td>
</tr>
<tr>
<td>Sign score = 0, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 16</td>
<td>0</td>
<td>50 (20.2)c</td>
<td>32 (11.7)b</td>
<td>0</td>
<td>86 (20.9)a</td>
</tr>
</tbody>
</table>

a p < 0.001 for comparison between guselkumab and placebo.
b comparisons between guselkumab and adalimumab were not performed.
c p < 0.001 for comparison between guselkumab and placebo for major secondary endpoints.

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 among subjects randomized to maintenance therapy at Week 28.
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 ≥ 2) to ustekinumab at Week 16. All patients (N=871) received open-label ustekinumab (45 mg ≤100 kg and 90 mg >100 kg) at Weeks 0 and 4. At Week 16, 268 patients with an IGA ≥ 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 randomized subjects were similar to those observed in VOYAGE 1 and 2.

After randomization, 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 ≥ 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 ≥ 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 ≥ 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 2).

No new safety findings were observed in patients who switched from ustekinumab to guselkumab.

**Figure 2:** 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

Paediatric population
The European Medicines Agency has deferred the obligation to submit the results of studies with Tremfya in plaque psoriasis 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 (± SD) maximum serum concentration ($C_{\text{max}}$) of 8.09 ± 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 (± SD) steady-state trough serum guselkumab concentrations in two phase III studies were 1.15 ± 0.73 mcg/mL and 1.23 ± 0.84 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.

Linearity/non-linearity
The systemic exposure of guselkumab ($C_{\text{max}}$ 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 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. Population pharmacokinetic analyses indicated there were no apparent changes in CL/F estimate in patients ≥ 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 $C_{\text{max}}$ 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 in the outer carton in order to protect from light.

6.5 Nature and contents of container

1 mL solution in a pre-filled glass syringe with a fixed needle and a needle shield, assembled in an automatic needle guard. Guselkumab is available in a pack containing one pre-filled syringe.

6.6 Special precautions for disposal and other handling

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

Prior to use, a visual inspection of the pre-filled syringe 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.
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

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

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 AUTHORIZATION

• Periodic safety update reports

The requirements for submission of periodic safety update reports 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 shall submit the first periodic safety update report 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 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
<table>
<thead>
<tr>
<th>PARTICULARS TO APPEAR ON THE OUTER PACKAGING</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRE-FILLED SYRINGE CARTON TEXT (100 mg)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1. NAME OF THE MEDICINAL PRODUCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tremfya 100 mg solution for injection</td>
</tr>
<tr>
<td>guselkumab</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. STATEMENT OF ACTIVE SUBSTANCE(S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Each pre-filled syringe contains 100 mg of</td>
</tr>
<tr>
<td>guselkumab in 1 mL.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. LIST OF EXCIPIENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excipients: sucrose, histidine, histidine</td>
</tr>
<tr>
<td>monohydrochloride monohydrate, polysorbate</td>
</tr>
<tr>
<td>80, water for injections.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. PHARMACEUTICAL FORM AND CONTENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solution for injection</td>
</tr>
<tr>
<td>1 pre-filled syringe</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. METHOD AND ROUTE(S) OF ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do not shake</td>
</tr>
<tr>
<td>Subcutaneous use</td>
</tr>
<tr>
<td>Read the package leaflet before use.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keep out of the sight and reach of children.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7. OTHER SPECIAL WARNING(S), IF NECESSARY</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>8. EXPIRY DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXP</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>9. SPECIAL STORAGE CONDITIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Store in a refrigerator.</td>
</tr>
<tr>
<td>Do not freeze.</td>
</tr>
</tbody>
</table>
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:
<table>
<thead>
<tr>
<th>1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION</th>
</tr>
</thead>
</table>
| 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
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.

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.

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.

Look out for infections and allergic reactions
Tremfya may lower your ability to fight infections and may therefore increase your risk of infections and allergic reactions. Tell your doctor or seek medical help immediately if you notice any signs of an infection or an allergic reaction while you are taking Tremfya. Such signs are listed below.

Infections
- 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
- diarrhea or stomach pain
- warm, red, or painful skin or sores on your body which are different from your psoriasis
- cough
- diarrhea or stomach pain
- shortness of breath
- warm, red, or painful skin or sores on your body which are different from your psoriasis
- burning when you urinate or urinating more often than usual

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

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.

- 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.

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, symptoms of psoriasis may come back.

4. **Possible side effects**

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

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):
- upper respiratory infections

Some side effects are common (may affect up to 1 in 10 people):
- headache
- joint pain (arthralgia)
- diarrhoea
- stomach flu (gastroenteritis)
- redness at the injection site
- hives
- fungal infection of the skin, for instance between the toes (e.g., athlete’s foot)
- herpes simplex infections

Some side effects are uncommon (may affect up to 1 in 100 people):
- pain at the injection site

**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 of 1 mL.

**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"
Geležinio Vilko g. 18A
LT-08104 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

Česká republika
Janssen-Cilag s.r.o.
Karla Enliššé 3201/06
CZ-150 00 Praha 5 - Smíchov
Tel.: +420 227 012 227

Danmark
Janssen-Cilag A/S
Bregnerødvej 133
DK-3460 Birkerød
Tlf: +45 45 94 82 82

Deutschland
Janssen-Cilag GmbH
Johnson & Johnson Platz 1
D-41470 Neuss
Tel: +49 2137 955 955

Eesti
UAB "JOHNSON & JOHNSON" Eesti filiaal
Lõõtsa 2
EE-11415 Tallinn
Tel: +372 617 7410

Ελλάδα
Janssen-Cilag Φαρμακευτική Α.Ε.Β.Ε.
Λεωφόρος Ειρήνης 56
GR-151 21 Πεύκη, Αθήνα
Τηλ: +30 210 80 90 000

España
Janssen-Cilag, S.A.
Paseo de las Doce Estrellas, 5-7
E-28042 Madrid
Tel: +34 91 722 81 00

France
Janssen-Cilag
1, rue Camille Desmoulins, TSA 91003
F-92787 Issy Les Moulineaux, Cedex 9
Tél: 0 800 25 50 75 / +33 1 55 00 40 03

Hrvatska
Johnson & Johnson S.E. d.o.o.
Oreškovićeva 6h
10010 Zagreb
Tel: +385 1 6610 700

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

Magyarország
Janssen-Cilag Kft.
Nagyenyed u. 8-14
H-Budapest, 1123
Tel.: +36 1 884 2858

Malta
AM MANGION LTD.
Mangion Building, Triq Ġdida fi Triq Valletta
MT-Hal-Luqa LQA 6000
Tel: +356 2397 6000

Nederland
Janssen-Cilag B.V.
Graaf Engelbertlaan 75
NL-4837 DS Breda
Tel: +31 76 711 1111

Norge
Janssen-Cilag AS
Postboks 144
NO-1325-Lysaker
Tlf: +47 24 12 65 00

Österreich
Janssen-Cilag Pharma GmbH
Vorgartenstrasse 206B
A-1020 Wien
Tel: +43 1 6610 300

Polska
Janssen-Cilag Polska Sp. z o.o.
ul. Ilżecka 24
PL-02-135 Warszawa
Tel.: +48 22 237 60 00

Portugal
Janssen-Cilag Farmacêutica, Lda.
Estrada Consigliieri Pedroso, 69 A
Queluz de Baixo
PT-2734-503 Barcarena
Tel: +351 21 43 68 835

România
Johnson & Johnson România SRL
Str. Tipografilor nr. 11-15
Clădirea S-Park, Corp B3-B4, Etaj 3
013714 București, ROMÂNIA
Tel: +40 21 207 1800
Ireland
Janssen-Cilag Ltd.
50-100 Holmers Farm Way
High Wycombe
Buckinghamshire HP12 4EG
United Kingdom
Tel: +44 1 494 567 444

Slovenija
Johnson & Johnson d.o.o.
Šmartinska cesta 53
SI-1000 Ljubljana
Tel: +386 1 401 18 30

Ísland
Janssen-Cilag AB
c/o Vistor hf.
Hörgatúni 2
IS-210 Gardabær
Sími: +354 535 7000

Slovenská republika
Johnson & Johnson, s.r.o.
CBC III, Karadžičova 12
SK-821 08 Bratislava
Tel: +421 232 408 400

Italia
Janssen-Cilag SpA
Via M.Buonarroti, 23
I-20093 Cologno Monzese MI
Tel: +39 02 2510 1

Suomi/Finland
Janssen-Cilag Oy
Vaisalantie/Vaisalavägen 2
FI-02130 Espoo/Esbo
Puh/Tel: +358 207 531 300

Κύπρος
Βαρνάβας Χατζηπαναγής Λτδ
Λεωφόρος Γιάννου Κρανιδιώτη 226
Λατσιά
CY-2234 Λευκωσία
Tηλ: +357 22 207 700

Sverige
Janssen-Cilag AB
Box 4042
SE-16904 Solna
Tel: +46 8 626 50 00

Latvija
UAB "JOHNSON & JOHNSON" filiāle Latvijā
Mākusālas iela 101
Rīga, LV-1004
Tel: +371 678 93561

United Kingdom
Janssen-Cilag Ltd.
50-100 Holmers Farm Way
High Wycombe
Buckinghamshire HP12 4EG - UK
Tel: +44 1 494 567 444

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Detailed information on this medicine is available on the European Medicines Agency web site:
Instructions for use
Tremfya
Pre-filled syringe

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

Plunger
Do not hold or pull plunger at any time.

Safety guard

Finger flange

Body
Hold syringe body below finger flange.

Viewing window

Needle cover
Do not remove until you are ready to inject Tremfya (See Step 2).
After injection

Plunger locks

Safety guard activates

Needle retracts into the body

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.