HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TREMFYA™ safely and effectively. See full prescribing information for TREMFYA.

TREMFYA (guselkumab) injection, for subcutaneous use
Initial U.S. Approval: 2017

----------INDICATIONS AND USAGE----------

TREMFYA is an interleukin-23 blocker indicated for the treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. (1)

----------DOSAGE AND ADMINISTRATION----------

100 mg administered by subcutaneous injection at Week 0, Week 4 and every 8 weeks thereafter (2.1)

----------DOSAGE FORMS AND STRENGTHS----------

Injection: 100 mg/mL in a single-dose prefilled syringe. (3)

----------CONTRAINDICATIONS----------

None (4)

----------WARNINGS AND PRECAUTIONS----------

- Infections: TREMFYA may increase the risk of infection. Instruct patients to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur. If a serious infection develops, discontinue TREMFYA until the infection resolves. (5.1)
- Tuberculosis (TB): Evaluate for TB prior to initiating treatment with TREMFYA. (5.2)

----------ADVERSE REACTIONS----------

Most common (≥1%) adverse reactions associated with TREMFYA include upper respiratory infections, headache, injection site reactions, arthralgia, diarrhea, gastroenteritis, tinea infections, and herpes simplex infections. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Janssen Biotech, Inc. at 1-800-JANSSEN (1-800-526-7736) or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

----------DRUG INTERACTIONS----------

Avoid use of live vaccines in patients treated with TREMFYA. (7.1)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 07/2017

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

TREMFYA™ is indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage

TREMFYA is administered by subcutaneous injection. The recommended dose is 100 mg at Week 0, Week 4, and every 8 weeks thereafter.

2.2 Tuberculosis Assessment Prior to Initiation of TREMFYA

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with TREMFYA *[see Warnings and Precautions (5.2)]*.

2.3 Important Administration Instructions

Administer TREMFYA subcutaneously. Each prefilled syringe is for single-dose only. Instruct patients to inject the full amount (1 mL), which provides 100 mg of TREMFYA.

Do not inject TREMFYA into areas where the skin is tender, bruised, red, hard, thick, scaly, or affected by psoriasis *[see Instructions for Use]*.

TREMFYA is intended for use under the guidance and supervision of a physician. TREMFYA may be administered by a health care professional, or a patient may self-inject after proper training in subcutaneous injection technique.

The TREMFYA *Instructions for Use* contains more detailed patient instructions on the preparation and administration of TREMFYA *[see Instructions for Use]*.

2.4 Preparation for Use of TREMFYA Prefilled Syringe

Before injection, remove TREMFYA prefilled syringe from the refrigerator and allow TREMFYA to reach room temperature (30 minutes) without removing the needle cap.

Inspect TREMFYA visually for particulate matter and discoloration prior to administration. TREMFYA is a clear and colorless to light yellow solution that may contain small translucent particles. Do not use if the liquid contains large particles, is discolored or cloudy. TREMFYA does not contain preservatives; therefore, discard any unused product remaining in the prefilled syringe.

3 DOSAGE FORMS AND STRENGTHS

Injection: 100 mg/mL in a single-dose prefilled syringe

TREMFYA is a clear and colorless to light yellow solution that may contain small translucent particles.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Infections

TREMFYA may increase the risk of infection. In clinical trials, infections occurred in 23% of subjects in the TREMFYA group versus 21% of subjects in the placebo group through 16 weeks of treatment. Upper respiratory tract infections, gastroenteritis, tinea infections, and herpes simplex infections occurred more frequently in the TREMFYA group than in the placebo group *[see Adverse Reactions (6.1)]*. The rate of serious infections for the TREMFYA group and the placebo group was ≤ 0.2%. Treatment with TREMFYA should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated.

In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing TREMFYA. Instruct patients to seek medical help if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops a clinically important or serious infection or is not responding to standard therapy, monitor the patient closely and discontinue TREMFYA until the infection resolves.

5.2 Pre-treatment Evaluation for Tuberculosis

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with TREMFYA. Initiate treatment of latent TB prior to administering TREMFYA. In clinical studies, 105 subjects with latent TB who were concurrently treated with TREMFYA and appropriate TB prophylaxis did not develop active TB (during the mean follow-up of 43 weeks). Monitor patients for signs and symptoms of active TB during and after TREMFYA treatment. Consider anti-TB therapy 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. Do not administer TREMFYA to patients with active TB infection.

5.3 Immunizations

Prior to initiating therapy with TREMFYA, consider completion of all age appropriate immunizations according to current immunization guidelines. Avoid use of live vaccines in patients treated with TREMFYA. No data are available on the response to live or inactive vaccines.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of labeling:

- Infections *[see Warnings and Precautions (5.1)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In clinical trials, a total of 1748 subjects with moderate-to-severe plaque psoriasis received TREMFYA. Of these, 1393 subjects were exposed to TREMFYA for at least 6 months and 728 subjects were exposed for at least 1 year.

Data from two placebo- and active-controlled trials (VOYAGE 1 and VOYAGE 2) in 1441 subjects (mean age 44 years; 70% males; 82% white) were pooled to evaluate the safety of TREMFYA (100 mg administered subcutaneously at Weeks 0 and 4, followed by every 8 weeks).

Weeks 0 to 16

In the 16-week placebo-controlled period of the pooled clinical trials (VOYAGE 1 and VOYAGE 2), adverse events occurred in 49% of subjects in the TREMFYA group compared to 47% of subjects in the placebo group and 49% of subjects in the U.S. licensed adalimumab group. Serious adverse events occurred in 1.9% of the TREMFYA group (6.3 events per 100 subject-years of follow-up) compared to 1.4% of the placebo group (4.7 events per 100 subject-years of follow-up), and in 2.6% of U.S. licensed adalimumab group (9.9 events per 100 subject-years of follow-up).

Table 1 summarizes the adverse reactions that occurred at a rate of at least 1% and at a higher rate in the TREMFYA group than in the placebo group during the 16-week placebo-controlled period.

Table 1: Adverse Reactions Occurring in ≥1% of Subjects through Week 16 in VOYAGE 1 and VOYAGE 2

	TREMFYA[a] 100 mg N=823 n (%)	**Adalimumab[b] N=196 n (%)**	**Placebo N=422 n (%)**
Upper respiratory infections[c]	118 (14.3)	21 (10.7)	54 (12.8)
Headache[d]	38 (4.6)	2 (1.0)	14 (3.3)
Injection site reactions[e]	37 (4.5)	15 (7.7)	12 (2.8)
Arthralgia	22 (2.7)	4 (2.0)	9 (2.1)
Diarrhea	13 (1.6)	3 (1.5)	4 (0.9)
Gastroenteritis[f]	11 (1.3)	4 (2.0)	4 (0.9)
Tinea infections[g]	9 (1.1)	0	0
Herpes simplex infections[h]	9 (1.1)	0	2 (0.5)

[a] subjects receiving 100 mg of TREMFYA at Week 0, Week 4, and every 8 weeks thereafter
[b] U.S. licensed adalimumab
[c] Upper respiratory infections include nasopharyngitis, upper respiratory tract infection (URTI), pharyngitis, and viral URTI.
[d] Headache includes headache and tension headache.
[e] Injection site reactions include injection site erythema, bruising, hematoma, hemorrhage, swelling, edema, pruritus, pain, discoloration, induration, inflammation, and urticaria.
[f] Gastroenteritis includes gastroenteritis and viral gastroenteritis.

[g] Tinea infections include tinea pedis, tinea cruris, tinea infection, and tinea manuum infections.
[h] Herpes simplex infections include oral herpes, herpes simplex, genital herpes, genital herpes simplex, and nasal herpes simplex.

Adverse reactions that occurred in < 1% but > 0.1% of subjects in the TREMFYA group and at a higher rate than in the placebo group through Week 16 in VOYAGE 1 and VOYAGE 2 were migraine, candida infections, and urticaria.

Specific Adverse Reactions

Infections

Infections occurred in 23% of the TREMFYA group compared to 21% of the placebo group.

The most common (≥ 1%) infections were upper respiratory infections, gastroenteritis, tinea infections, and herpes simplex infections; all cases were mild to moderate in severity and did not lead to discontinuation of TREMFYA.

Elevated Liver Enzymes

Elevated liver enzymes were reported more frequently in the TREMFYA group (2.6%) than in the placebo group (1.9%). Of the 21 subjects who were reported to have elevated liver enzymes in the TREMFYA group, all events except one were mild to moderate in severity and none of the events led to discontinuation of TREMFYA.

Safety through Week 48

Through Week 48, no new adverse reactions were identified with TREMFYA use and the frequency of the adverse reactions was similar to the safety profile observed during the first 16 weeks of treatment.

6.2 Immunogenicity

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

Up to Week 52, approximately 6% of subjects treated with TREMFYA developed antidrug antibodies. Of the subjects who developed antidrug antibodies, approximately 7% had antibodies that were classified as neutralizing antibodies. Among the 46 subjects who developed antibodies to guselkumab and had evaluable data, 21 subjects exhibited lower trough levels of guselkumab, including one subject who experienced loss of efficacy after developing high antibody titers. However, antibodies to guselkumab were generally not associated with changes in clinical response or development of injection-site reactions.

7 DRUG INTERACTIONS

7.1 Live Vaccinations

Avoid use of live vaccines in patients treated with TREMFYA *[see Warnings and Precautions (5.3)]*.

7.2 CYP450 Substrates

The formation of CYP450 enzymes can be altered by increased levels of certain cytokines (e.g., IL-1, IL-6, IL-10, TNFα, interferon) during chronic inflammation.

Results from an exploratory drug-drug interaction study in subjects with moderate-to-severe psoriasis suggested a low potential for clinically relevant drug interactions for drugs metabolized by CYP3A4, CYP2C9, CYP2C19 and CYP1A2 but the interaction potential cannot be ruled out for drugs metabolized by CYP2D6. However, the results were highly variable because of the limited number of subjects in the study.

Upon initiation of TREMFYA in patients who are receiving concomitant CYP450 substrates, particularly those with a narrow therapeutic index, consider monitoring for therapeutic effect or drug concentration and consider dosage adjustment as needed *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on TREMFYA use in pregnant women to inform a drug associated risk of adverse developmental outcomes. Human IgG antibodies are known to cross the placental barrier; therefore, TREMFYA may be transmitted from the mother to the developing fetus. In a combined embryofetal development and pre- and post-natal development study, no adverse developmental effects were observed in infants born to pregnant monkeys after subcutaneous administration of guselkumab during organogenesis through parturition at doses up to 30 times the maximum recommended human dose (MRHD). Neonatal deaths were observed at 6- to 30-times the MRHD *(see Data)*. The clinical significance of these nonclinical findings is unknown.

All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

In a combined embryofetal development and pre- and post-natal development study, pregnant cynomolgus monkeys were administered weekly subcutaneous doses of guselkumab up to

50 mg/kg (30 times the MRHD based on a mg/kg comparison) from the beginning of organogenesis to parturition. Neonatal deaths occurred in the offspring of one control monkey, three monkeys administered guselkumab at 10 mg/kg/week (6 times the MRHD based on a mg/kg comparison) and three monkeys administered guselkumab at 50 mg/kg/week (30 times the MRHD based on a mg/kg comparison). The clinical significance of these findings is unknown. No guselkumab-related effects on functional or immunological development were observed in the infants from birth through 6 months of age.

8.2 Lactation

Risk Summary

There are no data on the presence of guselkumab in human milk, the effects on the breastfed infant, or the effects on milk production. Guselkumab was not detected in the milk of lactating cynomolgus monkeys. Maternal IgG is known to be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TREMFYA and any potential adverse effects on the breastfed infant from TREMFYA or from the underlying maternal condition.

8.4 Pediatric Use

The safety and efficacy of TREMFYA in pediatric patients (less than 18 years of age) have not been established.

8.5 Geriatric Use

Of the 1748 subjects with plaque psoriasis exposed to TREMFYA, a total of 93 subjects were 65 years or older, and 4 subjects were 75 years or older. No overall differences in safety or effectiveness were observed between older and younger subjects who received TREMFYA. However, the number of subjects aged 65 years and older was not sufficient to determine whether they respond differently from younger subjects *[see Clinical Pharmacology (12.3)]*.

10 OVERDOSAGE

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

11 DESCRIPTION

Guselkumab, an interleukin-23 blocker, is a human immunoglobulin G1 lambda (IgG1λ) monoclonal antibody. Guselkumab is produced in a mammalian cell line using recombinant DNA technology.

TREMFYA (guselkumab) Injection is a sterile, preservative free, clear, colorless to light yellow solution that may contain small translucent particles. Each single-dose prefilled syringe for subcutaneous use contains 100 mg of guselkumab in 1 mL. TREMFYA is supplied as a single-dose solution in a 1 mL glass syringe with a 27G, half inch fixed needle assembled in a passive needle guard delivery system.

Each TREMFYA prefilled syringe delivers 1 mL of solution containing guselkumab (100 mg), L-histidine (0.6 mg), L-histidine monohydrochloride monohydrate (1.5 mg), polysorbate 80 (0.5 mg), sucrose (79 mg) and water for injection at pH 5.8.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Guselkumab is a human monoclonal IgG1λ antibody that selectively binds to the p19 subunit of interleukin 23 (IL-23) and inhibits its interaction with the IL-23 receptor. IL-23 is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Guselkumab inhibits the release of proinflammatory cytokines and chemokines.

12.2 Pharmacodynamics

Guselkumab reduced serum levels of IL-17A, IL-17F and IL-22 relative to pretreatment levels in evaluated subjects with psoriasis based on exploratory analysis of the pharmacodynamic markers. The relationship between these pharmacodynamic markers and the mechanism(s) by which guselkumab exerts its clinical effects is not fully understood.

12.3 Pharmacokinetics

Guselkumab exhibited linear pharmacokinetics in healthy subjects and subjects with psoriasis following subcutaneous injections. In subjects with psoriasis, following subcutaneous administration of 100 mg of TREMFYA at Weeks 0 and 4, and every 8 weeks thereafter, mean steady-state trough serum guselkumab concentration was approximately 1.2 mcg/mL.

Absorption

Following a single 100 mg subcutaneous injection in healthy subjects, guselkumab reached a mean (± SD) maximum serum concentration of 8.09 ± 3.68 mcg/mL by approximately 5.5 days post dose. The absolute bioavailability of guselkumab following a single 100 mg subcutaneous injection was estimated to be approximately 49% in healthy subjects.

Distribution

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

Elimination

Apparent clearance in subjects with plaque psoriasis was 0.516 L/day. Mean half-life of guselkumab was approximately 15 to 18 days in subjects with plaque psoriasis across studies.

Metabolism

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

Specific Populations

No apparent differences in clearance were observed in subjects ≥ 65 years of age compared to subjects < 65 years of age, suggesting no dose adjustment is needed for elderly patients. Clearance and volume of distribution of guselkumab increases as body weight increases, however, observed clinical trial data indicate that dose adjustment for body weight is not warranted. No specific studies have been conducted to determine the effect of renal or hepatic impairment on the pharmacokinetics of guselkumab.

Drug Interactions

Population pharmacokinetic analyses indicated that concomitant use of ibuprofen, acetylsalicylic acid, or acetaminophen did not affect the clearance of guselkumab.

Cytochrome P450 Substrates

The effects of guselkumab on the pharmacokinetics of midazolam (metabolized by CYP3A4), warfarin (metabolized by CYP2C9), omeprazole (metabolized by CYP2C19), dextromethorphan (metabolized by CYP2D6), and caffeine (metabolized by CYP1A2) were evaluated in an exploratory study with 6 to 12 evaluable subjects with moderate-to-severe plaque psoriasis. Changes in AUC_{inf} of midazolam, S-warfarin, omeprazole, and caffeine after a single dose of guselkumab were not clinically relevant. For dextromethorphan, changes in AUC_{inf} after guselkumab were not clinically relevant in 9 out of 10 subjects; however, a 2.9-fold change in AUC_{inf} was observed in one individual *[see Drug Interactions (7.2)]*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been conducted to evaluate the carcinogenic or mutagenic potential of TREMFYA.

No effects on fertility parameters were observed after male guinea pigs were subcutaneously administered guselkumab at a dose of 25 mg/kg twice weekly (15 times the MRHD based on a mg/kg comparison).

No effects on fertility parameters were observed after female guinea pigs were subcutaneously administered guselkumab at doses up to 100 mg/kg twice-weekly (60 times the MRHD based on a mg/kg comparison).

14 CLINICAL STUDIES

Three multicenter, randomized, double-blind trials (VOYAGE 1 [NCT02207231], VOYAGE 2 [NCT02207244], and NAVIGATE [NCT02203032]) enrolled subjects 18 years of age and older with moderate-to-severe plaque psoriasis who were eligible for systemic therapy or phototherapy. Subjects had an Investigator's Global Assessment (IGA) score of ≥3 ("moderate") on a 5-point scale of overall disease severity, a Psoriasis Area and Severity Index (PASI) score ≥12, and a minimum affected body surface area (BSA) of 10%. Subjects with guttate, erythrodermic, or pustular psoriasis were excluded.

VOYAGE 1 and VOYAGE 2

In VOYAGE 1 and VOYAGE 2, 1443 subjects were randomized to either TREMFYA (100 mg at Weeks 0 and 4 and every 8 weeks thereafter), placebo or U.S. licensed adalimumab (80 mg at Week 0 and 40 mg at Week 1, followed by 40 mg every other week thereafter).

Both trials assessed the responses at Week 16 compared to placebo for the two co-primary endpoints:

- the proportion of subjects who achieved an IGA score of 0 ("cleared") or 1 ("minimal");
- the proportion of subjects who achieved at least a 90% reduction from baseline in the PASI composite score (PASI 90).

Comparisons between TREMFYA and U.S. licensed adalimumab were secondary endpoints at the following time points:

- at Week 16 (VOYAGE 1 and VOYAGE 2), the proportions of subjects who achieved an IGA score of 0 or 1, a PASI 90, and a PASI 75 response;
- at Week 24 (VOYAGE 1 and VOYAGE 2), and at Week 48 (VOYAGE 1), the proportions of subjects achieving an IGA score of 0, an IGA score of 0 or 1, and a PASI 90 response.

Other evaluated outcomes included improvement in psoriasis symptoms assessed on the Psoriasis Symptoms and Signs Diary (PSSD) and improvements in psoriasis of the scalp at Week 16.

In both trials, subjects were predominantly men and white, with a mean age of 44 years and a mean weight of 90 kg. At baseline, subjects had a median affected BSA of approximately 21%, a median PASI score of 19, and 18% had a history of psoriatic arthritis. Approximately 24% of subjects had an IGA score of severe. In both trials, 23% had received prior biologic systemic therapy.

Clinical Response

Table 2 presents the efficacy results at Week 16 in VOYAGE 1 and VOYAGE 2.

Table 2: Efficacy Results at Week 16 in Adults with Plaque Psoriasis (NRI[a])

	VOYAGE 1		VOYAGE 2	
Endpoint	**TREMFYA (N=329) n (%)**	**Placebo (N=174) n (%)**	**TREMFYA (N=496) n (%)**	**Placebo (N=248) n (%)**
IGA response of 0/1[b, c]	280 (85)	12 (7)	417 (84)	21 (8)
PASI 90 response[b]	241 (73)	5 (3)	347 (70)	6 (2)

[a] NRI = Non-Responder Imputation

[b] Co-Primary Endpoints

[c] IGA response of 0 (cleared) or 1 (minimal)

Table 3 presents the results of an analysis of all the North America sites (i.e., U.S. and Canada), demonstrating superiority of TREMFYA to U.S. licensed adalimumab.

Table 3: Efficacy Results in Adults with Plaque Psoriasis (NRI[a])

	VOYAGE 1 Trial 3001		VOYAGE 2 Trial 3002	
Endpoint	**TREMFYA (N=115)[b] n (%)**	**Adalimumab[c] (N=115)[b] n (%)**	**TREMFYA (N=160)[b] n (%)**	**Adalimumab[c] (N=81)[b] n (%)**
IGA response of 0/1 (cleared or minimal)				
Week 16	97 (84)	70 (61)	119 (74)	50 (62)
Week 24	97 (84)	62 (54)	119 (74)	46 (57)
Week 48	91 (79)	62 (54)	NA	NA
IGA response of 0 (cleared)				
Week 24	61 (53)	27 (23)	76 (48)	23 (28)
Week 48	54 (47)	28 (24)	NA	NA
PASI 75 response				
Week 16	105 (91)	80 (70)	132 (83)	51 (63)
PASI 90 response				
Week 16	84 (73)	47 (41)	102 (64)	34 (42)
Week 24	92 (80)	51 (44)	113 (71)	41 (51)
Week 48	84 (73)	53 (46)	NA	NA

[a] NRI = Non-Responder Imputation

[b] subjects from sites in the United States and Canada

[c] U.S. licensed adalimumab

An improvement was seen in psoriasis involving the scalp in subjects randomized to TREMFYA compared to placebo at Week 16.

Examination of age, gender, race, body weight, and previous treatment with systemic or biologic agents did not identify differences in response to TREMFYA among these subgroups.

Maintenance and Durability of Response

To evaluate maintenance and durability of response (VOYAGE 2), subjects randomized to TREMFYA at Week 0 and who were PASI 90 responders at Week 28 were re-randomized to either continue treatment with TREMFYA every 8 weeks or be withdrawn from therapy (i.e. receive placebo).

At Week 48, 89% of subjects who continued on TREMFYA maintained PASI 90 compared to 37% of subjects who were re-randomized to placebo and withdrawn from TREMFYA. For responders at Week 28 who were re-randomized to placebo and withdrawn from TREMFYA, the median time to loss of PASI 90 was approximately 15 weeks.

Patient Reported Outcomes

Greater improvements in symptoms of psoriasis (itch, pain, stinging, burning and skin tightness) at Week 16 in TREMFYA compared to placebo were observed in both trials based on the Psoriasis Symptoms and Signs Diary (PSSD). Greater proportions of subjects on TREMFYA compared to U.S. licensed adalimumab achieved a PSSD symptom score of 0 (symptom-free) at Week 24 in both trials.

NAVIGATE

NAVIGATE evaluated the efficacy of 24 weeks of treatment with TREMFYA in subjects (N=268) who had not achieved an adequate response, defined as IGA ≥2 at Week 16 after initial

treatment with U.S. licensed ustekinumab (dosed 45 mg or 90 mg according to the subject's baseline weight at Week 0 and Week 4). These subjects were randomized to either continue with U.S. licensed ustekinumab treatment every 12 weeks or switch to TREMFYA 100 mg at Weeks 16, 20, and every 8 weeks thereafter. Baseline characteristics for randomized subjects were similar to those observed in VOYAGE 1 and VOYAGE 2.

In subjects with an inadequate response (IGA ≥2 at Week 16 to U.S. licensed ustekinumab), greater proportions of subjects on TREMFYA compared to U.S. licensed ustekinumab achieved an IGA score of 0 or 1 with a ≥2 grade improvement at Week 28 (31% vs 14%, respectively; 12 weeks after randomization).

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How supplied

TREMFYA (guselkumab) Injection is a clear and colorless to light yellow solution that may contain small translucent particles. TREMFYA is supplied as a single-dose 100 mg/mL prefilled syringe:

- NDC CODE: 57894-640-01

16.2 Storage and Handling

TREMFYA is sterile and preservative-free. Discard any unused portion.

- Store in a refrigerator at 2ºC to 8ºC (36ºF to 46ºF)
- Store in original carton until time of use
- Protect from light until use.
- Do not freeze.
- Do not shake

17 PATIENT COUNSELING INFORMATION

Advise the patient and/or caregiver to read the FDA-approved patient labeling *(Medication Guide and Instructions for Use)* before starting TREMFYA therapy, and each time the prescription is renewed, as there may be new information they need to know.

Infections

Instruct patients of the importance of communicating any history of infections to the healthcare provider and contacting their healthcare provider if they develop any symptoms of an infection *[see Warnings and Precautions (5.1)]*.

Instruction on Injection Technique

Instruct the patient or caregivers to perform the first self-injection under the supervision and guidance of a qualified healthcare professional for proper training in subcutaneous injection

technique. Instruct patients who are self-administering to inject the full dose of TREMFYA *[see Medication Guide and Instructions for Use]*.

Instruct patients or caregivers in the technique of proper needle and syringe disposal. Needles and syringes should be disposed of in a puncture-resistant container. Advise patients and caregivers not to reuse needles or syringes.

Remind patients if they forget to take their dose of TREMFYA to inject their dose as soon as they remember. They should then take their next dose at the appropriate scheduled time.

Product of USA

Manufactured by:
Janssen Biotech, Inc
Horsham, PA 19044
US License No. 1864

Medication Guide
TREMFYA™ (trem fye´ ah)
(guselkumab)
injection, for subcutaneous use

What is the most important information I should know about TREMFYA?

TREMFYA may cause serious side effects, including:

Infections. TREMFYA is a medicine that may lower the ability of your immune system to fight infections and may increase your risk of infections. Your healthcare provider should check you for infections and tuberculosis (TB) before starting treatment with TREMFYA and may treat you for TB before you begin treatment with TREMFYA if you have a history of TB or have active TB. Your healthcare provider should watch you closely for signs and symptoms of TB during and after treatment with TREMFYA.

- Tell your healthcare provider right away if you have an infection or have symptoms of an infection, including:
  - fever, sweats, or chills
  - cough
  - shortness of breath
  - blood in your phlegm (mucus)
  - muscle aches
  - warm, red, or painful skin or sores on your body different from your psoriasis
  - weight loss
  - diarrhea or stomach pain
  - burning when you urinate or urinating more often than normal

See **"What are the possible side effects of TREMFYA?"** for more information about side effects.

What is TREMFYA?

TREMFYA is a prescription medicine used to treat adults with moderate to severe plaque psoriasis who may benefit from taking injections or pills (systemic therapy) or phototherapy (treatment using ultraviolet or UV light).

It is not known if TREMFYA is safe and effective in children under 18 years of age.

Before using TREMFYA, **tell your healthcare provider about all of your medical conditions, including if you:**

- have any of the conditions or symptoms listed in the section **"What is the most important information I should know about TREMFYA?"**
- have an infection that does not go away or that keeps coming back.
- have TB or have been in close contact with someone with TB.
- have recently received or are scheduled to receive an immunization (vaccine). You should avoid receiving live vaccines during treatment with TREMFYA.
- are pregnant or plan to become pregnant. It is not known if TREMFYA can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if TREMFYA passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I use TREMFYA?

See the detailed "Instructions for Use" that comes with TREMFYA for information on how to prepare and inject a dose of TREMFYA, and how to properly throw away (dispose of) used TREMFYA prefilled syringes.

- Use TREMFYA exactly as your healthcare provider tells you to use it.
- If you miss your TREMFYA dose, inject a dose as soon as you remember. Then, take your next dose at your regular scheduled time. Call your healthcare provider if you are not sure what to do.

If you inject more TREMFYA than prescribed, call your healthcare provider right away.

What are the possible side effects of TREMFYA?

TREMFYA may cause serious side effects. See "What is the most important information I should know about TREMFYA?"

The most common side effects of TREMFYA include:

- upper respiratory infections
- joint pain (arthralgia)
- fungal skin infections
- headache
- diarrhea
- herpes simplex infections
- injection site reactions
- stomach flu (gastroenteritis)

These are not all the possible side effects of TREMFYA. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of TREMFYA

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use TREMFYA for a condition for which it was not prescribed. Do not give TREMFYA to other people, even if they have the same symptoms that you have. It may harm them. You can ask your healthcare provider or pharmacist for information about TREMFYA that is written for health professionals.

Manufactured by: Janssen Biotech, Inc., Horsham, PA 19044 U.S. License Number 1864
For more information, call 1-800-526-7736 or go to www.tremfyainfo.com.
This Medication Guide had been approved by the U.S. Food and Drug Administration. Approved: July/2017